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THE MEDICAL ASPECTS OF MUSTARD GAS POISONING

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WITH 156 ORIGINAL ILLUSTRATIONS

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TO

WILLIAM J. LYSTER,
Colonel, Medical Corps, U. S. A.

and

HAROLD C. BRADLEY,
Major, Chemical Warfare Service, U. S. A.

In Recognition of Pleasant Associations With the Medical
Advisory Board of the Chemical Warfare Service

PREFACE

The investigations on Dichlorethylsulphide (Mustard Gas) Poisoning recorded in this volume were begun as an independent war research problem in the Pathological Laboratory of the Medical Department of the University of Michigan in 1917. The Laboratory later, through Dr. Warthin, became associated with the Medical Advisory Board of the Chemical Warfare Service and abstracts and preliminary reports of these investigations are included in the Reports of that Department of the Service. Six articles, forming the nucleus of the investigation, were published in the Journal of Laboratory and Clinical Medicine, as follows: Pathology of the Skin Lesions, May, 1918; Pathology of the Ocular Lesions, October, 1918; The Treatment of Dichlorethylsulphide Injuries, ibid; The Clinical Pathology of Dichlorethylsulphide Poisoning, November, 1918; Lesions of the Respiratory and Gastrointestinal Tracts, February, 1919; The General Pathology of Mustard Gas (Dichlorethylsulphide) Poisoning, ibid. These articles have now been gathered together, corrected and expanded to form the chief part of the present volume. To this material we have added an introductory chapter on the Medical Aspects of Gassing in Warfare and a complete Bibliography of the Literature on Gassing in Warfare. We also have added a number of new and important illustrations.

The entire research has been carried through in a period of eighteen months, in a most intensive manner, involving an immense amount of labor. Its success was made possible only through the enthusiastic cooperation of the entire Laboratory Staff. Through Col. W. J. Lyster and Major H. C. Bradley of the Chemical Warfare Service we were given the opportunity of studying human material in one of the industrial plants concerned in the manufacture of mustard gas; and through the cooperation of the Chemical Warfare Service we were enabled to place at this plant a member of the Laboratory Staff, Dr. George R. Herrmann, thus making possible a collection of laboratory data in human cases, which is published as Chapter VI of this volume. We are also indebted to Captain L. L. Roos for the opportunity of studying the cases clinically and of performing an autopsy upon one of the fatal cases. To Major Moses Gomberg, Professor of Chemistry in the University of Michigan we owe first of all our thanks, as he, in the beginning, furnished us with a quantity of the purest mustard gas we were able to obtain from any source. With the dichlorethylsulphide made by him we have been able to standardize our entire series of investigations; at the same time we have compared its action with that of samples less pure, obtained from the Chemical Warfare Service and elsewhere. To Dr. Gomberg we are also indebted for a quantity of pure dihydroxyethylsulphide. To the Regents of the University of Michigan we are also grateful for a special grant of funds for necessary expenditures for animals and for additional technical assistance. Finally, we wish to give appreciative thanks to Dr. Harriet Taylor for her valuable services in the Laboratory and to Miss Frances Dunbar for her care and skill in printing our photomicrographic plates.

Aldred Scott Warthin,
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THE MEDICAL ASPECTS
OF
MUSTARD GAS POISONING

CHAPTER I

THE MEDICAL ASPECTS OF GASSING IN WARFARE

Introduction

That poison gas should have played such a prominent rôle as a weapon of warfare in the great war, as to cause this to be styled the "Chemical War," was not a matter to occasion feelings of shock or surprise. "German Gas" is but the logical evolutionary successor of "Greek Fire" and the Chinese "Stink-ball" or "Stink-pot."

"The fashion of Greek fire was such that it came to us as great as a tun of verjuice, and the fiery tail of it was as big as a mighty lance; it made such noise in the coming that it seemed like the thunder from heaven; and looked like a dragon flying through the air; so great a light did it throw that throughout the host men saw as though it were day for the light of them." *Jean de Joinville* (1224-1319).

Between the simple combinations of pitch, resin, sulphur, naphtha and quicklime, used in these primitive efforts to terrify and to conquer, and the chlorine, phosgene and mustard gas of the German gas attack, there lies the evolution of the science of chemistry and the chemical laboratory. If there is to be warfare, it is but logical that the contestants avail themselves of all the resources of human knowledge in order to win the struggle. So reasoned the German megalomaniac, on setting out to conquer the world.

"In the matter of making an end of the enemies' forces by violence, it is an incontestable and self-evident rule that the right of killing and annihilating, in regard to the hostile combatants is inherent in the warpower, and its organs, that all means which modern inventions afford, including the fullest, most dangerous and most massive means of destruction, may be utilized. These last, just because they attain the object of war as quickly as possible, are on that account to be regarded as indispensable and, when closely considered, the most humane." (*German War Book. Quotation from Military Surgeon,* 1915, xxxvii, p. 422.)

This is the science of war. To the German people, *de*-moralized by its saturation with such psychology, this became also the morals of warfare. All of the achievements of the physical sciences, the submarine, air-machine, explosive and incendiary bomb, and poison gas were to them agents to be used for the destruction of non-German human beings, and not for the advancement of the races of men in general. To such a prostitution of science it was but logical that bestial ruthlessness should be added.

German scientists, German university professors and chemists, were the instigators and promoters of the poison war. The names of Nernst, Professor of Chemistry at the University of Berlin, and Haber of the Berlin Chemical Institute should not be forgotten in this connection. Nor should that of any other university professor who signed the famous confession of perverted morals and psychology.

That poison gas came to play such an important part in the German attempt to overthrow the world did not occasion surprise to a small number of scientific minds outside of Germany. Its use was predicted before 1899; and at the Hague Conference of July 21, 1899, all the great powers agreed that no projectiles should be used "having as their sole object the diffusion of asphyxiating or deleterious gases."

The one surprising thing about the present war, to the scientist, is the apparent failure of Germany to make it a "disease" as well as a poison war. To what extent German medical scientists may have attempted the dissemination of infective agents among the allied forces we do not know; but it would have been out of keeping with their conception of ruthlessness not to have tried out this method. If such attempts were made they were apparently not successful enough to attract attention, or possibly the fear of the spread of infection, once started, into their own lines, may have limited their efforts in this direction.

Nevertheless, in spite of predictions and the certainty that the use of gas was a German possibility, the first gas attack, made on April 22, 1915, on the northeastern part of the Ypres salient, came as an overwhelming surprise to the French and Canadian troops holding that sector of the line. The attack was described by a Canadian officer as follows:

"On Thursday, April 22, when I was in a support trench about 600 yards from the German lines, I saw first of all a white smoke rising from the German trenches to a height of about three feet; then in front of the white smoke appeared a greenish cloud, which drifted along the ground, not rising more than seven feet from the ground when it reached our first trenches. Men in these trenches were obliged to leave, and a number were killed by the effects of the gas."

As the greenish-yellow gas moved with the wind over the allied soldiers, filling the trenches as it came, the men caught by it were enveloped in a suffocating, irritant cloud that dropped them on the spot or forced them to run in a panic of agonized fear. The Canadian line was broken by this attack, but the German rush was stopped, after a loss to the allies of several thousand men, killed or captured, and sixty guns. *Spear* says that of the twelve thousand Canadians holding this sector only two thousand were alive five days later. Those who did not die on the field presented a frightful picture of suffering in the hospitals. *Haldane* describes the men as "lying struggling for breath and blue in the face. On examining the blood with the spectroscope and other means I ascertained that the blueness was not due to the presence of any abnormal pigment. There was nothing to account for the blueness (cyanosis) and struggle for air but the one fact that they were suffering from acute bronchitis, such as is caused by inhalation of an irritant gas. Their statements were that when in the trenches they had been overwhelmed by an irritant gas produced in front of the German trenches and carried toward them by a gentle breeze.

"One of them died shortly after our arrival. A postmortem examination was conducted in our presence by Lieutenant McNee, a pathologist by profession, of Glasgow University. An examination showed that death was due to acute bronchitis and its secondary effects. There was no doubt that the bronchitis and accompanying slow asphyxiation were due to the irritant gas.

"The symptoms and the other facts so far ascertained point to the use by the German troops of chlorine or bromine for purposes of asphyxiation."

There is no doubt now that the poison used in this first gas attack was liquid chlorine discharged from cylinders fitted with internal siphons, so that the entire contents of the cylinder could be emptied into the air as liquid chlorine in a few minutes. The expanding cloud of gas hugs the ground, and as it is carried along by the wind fills all depressions. The full effect of this attack was said to have been felt as far as 3,000 yards from the German trenches, and its odor was distinctly perceptible at a distance of three miles. It was estimated that the Germans must have had at least one cylinder containing forty-five pounds of liquid chlorine to every yard of front subjected to the attack. Other attacks followed, but from June to December, 1915, the direction of the wind being unfavorable to the Germans, the latter used no gas. On December 19, 1915, they again made a surprise gas attack on the Ypres salient, using this time a mixture of chlorine and phosgene, in a much stronger concentration than in the previous gas attacks. Because of the allied antigas preparations in the form of masks, the number of immediate casualties was small, but the effects of phosgene were apparent in the large number of cases of delayed poisoning, in that men who thought they had been but slightly gassed became ill or died some hours or days later.

During the gas attacks, because of a peculiar odor and a lacrimatory action upon the eyes, it was believed that some substance causing lacrimation was mixed with the chlorine; but it was soon discovered that gas shell containing xylyl bromide were being used. Rapid developments in the use of more poisonous gases, in greater quantities and greater concentrations, in successive surprise attacks, brought the German gas warfare, in 1916, to the apparent limit of development, in so far as "drift" or "cloud" gas is concerned. The last gas cloud attack upon the British occurred in August, 1916, and against the French, on April 23, 1917. As the gas cloud had become more poisonous and concentrated, the allied casualties grew less as the result of efficient masks, respirators and gas-defense instruction. During the remainder of the war the development of German gas warfare lay along the lines of increasing the efficiency of the gas shell; and no apparent limit to that development had been reached when fighting ceased. There is no limit to the number or size of the gas shell, or to the variety of the poison, in liquid or solid form, contained in them, and capable of being atomized by the explosion over the area of the burst. In the last year of the war, gas shell became the most important weapons of war. *Auld* states that some bombardments were composed entirely of gas shell; and that as many as a quarter of a million have been fired on the attacking front during twenty-four hours. He estimates that probably one-quarter of all German shell of all caliber were gas shell.

The effects of gas attacks upon the troops have been variously described. There is apparently no doubt that some of the greatest reverses suffered by the Allies were due entirely to the casualties and the loss of morale caused by gas. The demoralization caused by gas attacks was naturally most marked in the case of recent recruits, but it is said to have extended at times to the most seasoned veterans. Of the actual number of gas casualties occurring in the Allied Armies we are still in ignorance, and may remain so. The verbal statements of men returning from over-seas vary greatly, according to their individual experiences; but of the immense, if not predominating, importance of poison gas as a weapon of warfare, there is no doubt. To meet the dangers of this new weapon, the Gas Defense Service developed likewise in importance. Efficient methods of protection were devised and employed by the Allies for every new phase of the German gas offense. In this they showed greater ingenuity and skill than the Germans; and the boasted efficiency of the latter suffers in comparison.

The effect of the German poison warfare upon the non-Teutonic world was to excite horror and execration. But reason and necessity demanded retaliation in kind; and such a boomerang the Germans were getting in the last months of the war. Had not a premature armistice intervened this boomerang might have become a veritable agent of annihilation to the German Army; as it has been stated on good authority that the American Chemical Warfare Service holds the secret of a gas much more toxic than any used by the Germans, and that this gas would have been made available to the Allied Armies within a very short time.

Poison gas may never be used again as an agent of destruction, but only if wars cease. Gas warfare did not reach its complete development in this war; should any other rich and powerful nation again plunge the world into war, it will be utilized again in a fuller development. Such an event is possible as long as the Hun type of psychology persists anywhere upon the earth. National safety lies in a knowledge of all such agents of destruction and the methods of protection against them.

Gases Used in Warfare

It is very probable that the Germans made many experimental trials of a great variety of poisons and combinations of poisons in the development of their chemical warfare, in the attempt to find those that were the most toxic, easiest and cheapest to make, and most easily handled. We do not yet possess a complete knowledge of these experiments. The analysis of shell bearing the same marks showed at different times a great difference in the content and relative proportions. Undoubtedly some of this variation was camouflage in the attempt to mislead the experts of the Allied armies; but much of it was probably experimental. Moreover some of the substances found by analysis were accidental contaminations or by-products. Various writers (*Hill*, *Ceridalli*, *Gallo*, *Filippini*, *Vaughan*, and others) have compiled lists of toxic gases, the use of which in the war, has been either hypothetically assumed, or actually verified. These lists include acrolein, allyl-iso-thiocyanate, arsenic trichloride, arsine, bromacetone, bromacetic ether, bromethylmethylketone, bromide of benzyl, bromide of toluyl, bromide of xylyl, bromine, carbon monoxide, carbonyl chloride (phosgene), chloracetone, chlorine, chloropicrin, cyanogen, dichlorethylsulphide (mustard gas), dichlormethylether, dimethysulphate, diphenylchlorarsine, diphenylfluorarsine, ethyldichlorarsine, formaldehyde, hydrocyanic acid, hydrosulphuric acid, iodoacetic ether, iodacetone, methylchlorsulphonic acid, monochlormethylchloroformate (palite), nitrogen peroxide, phenyl-carbylamine chloride, phosphine, phosphorus trichloride, sulphur dioxide and trioxide, and trichlormethylchloroformate (diphosgene, superpalite).

Apparently, however, the poisons found to be most effective in gas warfare were: Bromethylmethylketone, carbonyl chloride (phosgene), chlorine, chloropicrin, dichlorethylsulphide (mustard gas, yprite, yperite), dichlormethylether, diphenylchlorarsine, ethyldichlorarsine, monochlormethylchloroformate (palite), trichlormethylchloroformate (diphosgene, superpalite), and xylyl bromide.

These gases were used, according to *Auld* and *Norris*, as follows:

1. Drift or cloud—Chlorine, phosgene and chlorine.
2. Shell—Phosgene (carbonyl chloride).
3. Shell—Sulphur trioxide.
4. T-shell—Xylyl bromide.
   Benzyl bromide.
   Toluyl bromide.
5. K-shell—Monochlormethylchloroformate (palite).
6. Green-Cross Shell—Trichlormethylchloroformate (diphosgene, superpalite).
   " " " Trichlormethylchloroformate with chloropicrin.
7. Yellow-Cross Shell—Dichlorethylsulphide (mustard gas, yperite, yprite).
8. Blue-Cross Shell—Diphenylchlorarsine.
9. Shell—Ethyldichlorarsine, 50 per cent; dichlormethylether, 50 per cent.
10. Shell—Bromethylmethylketone.
11. Shell—Dibromoketone.
12. Shell—Phenyl-carbylamine-chloride.
13. Shell—Allyl-iso-thiocyanate.
14 Hand Grenades—Bromacetone, bromine, chloracetone, chlorsulfonic acid, dimethyl sulfate, methylchlorsulfonic acid.

According to their special action these gases may be divided into *lacrimators* (xylyl bromide), *sternutators* (diphenylchlorarsine, ethyldichlorarsine), *respiratory irritants* (chlorine, chloropicrin, phosgene, palite, diphosgene, dichlorethylsulphide), *escharotics* (dichlorethylsulphide, diphenylfluorarsine, dichlormethylether), *systemic poisons* (arsine compounds).

It must not be forgotten that our knowledge is not absolutely definite upon the above points; and that even among writers on military gassing there is a notable confusion as to the use of some terms, notably of phosgene. Phosgene is carbonyl chloride; but *Auld* seems to confuse phosgene and palite (monochlormethylchloroformate) ; and *Norris* also uses palite as a synonym of phosgene. There is no relationship between phosgene (carbonyl chloride), palite (monochlormethylchloroformate) and diphosgene or superpalite (trichlormethylchloroformate). The psychology of the confusion seems explainable as follows: The condensed formula of superpalite or trichlormethylchloroformate ($C_2O_2Cl_4$) is doubly equivalent to that of phosgene ($COCl_2$), hence this substance has been erroneously called diphosgene. Palite, as distinguished from superpalite, has been, in still greater degree of error, called phosgene.

It has been stated that toward the close of the war the Germans were using an increasing amount of arsenical compounds, either alone, or in combination with other lethal gases, the primary object of the arsenical compound being to induce vomiting and thus leave the soldier exposed to the action of the other poison. In addition to their properties as sternutators, ''vomiting gases,'' and local escharotics, the arsenical poisons later exert a general poisonous action upon the blood, liver, kidneys, etc.

At the beginning of the war some of the poison gases were clinically unknown, and the pathologic action of the majority was but imperfectly worked out. Certain gases, as chlorine, had been classed as *irrespirable* or *irritant* gases, but the mode of action of these upon the internal organs was practically unknown. While these may produce death by their action upon the respiratory tract, they possess a toxic action for other tissues, as in the case of chlorine poisoning, in which death may be as immediate as in cases of poisoning with hydrocyanic acid. We are not yet sure of the mechanism of this toxic action of chlorine. The classification given above is, of course, based only upon one striking property shown by each particular gas, but does not consider all, or even the most important, of its toxic properties. The asphyxiating gases may possess a local escharotic action, or have a toxic action upon the blood, heart, kidneys or nervous system, as well. The lacrimatory gases may also act upon the respiratory tract, and have a general toxic action. It is, of course, evident, that in the selection of gases for military use, as far as toxic action is concerned, choice would fall especially upon those that would immediately incapacitate the soldier by their action upon eyes, respiratory tract, or blood in the pulmonary capillaries (lacrimatory, sneezing, vomiting, asphyxiating, and blood poisons). Poison gas could be used to cause temporary or permanent incapacitation, or to kill at once, or to bring about a delayed fatal ending. A gas, or combination of gases that would first cause the soldier to lose his morale and lead him to expose himself still further to the gas in order that a fatal action might be brought about would naturally be the one chosen, and in making such combinations the Germans showed an ingenuity that comes only from expert knowledge and training in the science of chemistry, and in the practical manufacture of chemical substances. Nevertheless, the range of poisons found by them to be suitable for gas warfare is a small one. The pathologic action of these, as far as our knowledge extends at the present time, is given below:

ARSENIC COMPOUNDS.—ARSINE, AsH_3, produces nausea, vomiting, metallic taste in mouth, burning in throat, diarrhea, prostration, headache, dizziness, tremor, extreme hemolysis, icterus, hematuria, suppression of urine, and death from the second to the sixth day. The symptoms come on very quickly after exposure; headache, vertigo and insomnia persist for several days. Tenderness and enlargement of the liver may be present. Mild cases may recover within fifteen days, only slight anemia and muscular weakness remaining. The essential pathologic features are those of acute arsenic poisoning: degenerative hepatitis and nephritis, icterus and hemolysis. DIPHENYLCHLORARSINE and ETHYLDICHLORARSINE were used primarily as sternutators. These substances produce the most violent and uncontrollable attacks of sneezing, described as "coming from the very bottom of your stomach upward, and feel as if the whole of your chest were going to come out with it." The sneezing is constant for a short time; and in mild cases there appear to be no after effects. In stronger concentrations irritation of the respiratory tract and bronchitis may be produced, with constitutional symptoms of arsenic poisoning, as in the case of arsine. Diphenylchlorarsine is said to be as toxic as phosgene. DIPHENYLFLUORARSINE is said to produce as marked a vesicating action as mustard gas but its effects are not so lasting. Had gas warfare continued, its further development would most probably have been in the use of new and more toxic arsenical compounds.

BROMINE AND BROMIDES.—Br, density as compared to air, 5.52. Boiling point, 59°. Although organic bromide compounds were used extensively, there is little evidence in the literature to indicate that bromine itself has ever been employed in gassing. Animal experimentation has been carried on with it in this connection, however, to an extent second only to that in the case of chlorine. *Symes*, and *Symes* and *Golla* using a high concentration of bromine vapor on pithed cats, found a marked obstruction of the air-way which they believed to be due in part to spasm of the bronchial musculature. Failing to relieve this by intravenous use of atropine, although the inhalation of stramonium fumes was consistently successful, they concluded that the bronchial circulation had been obstructed to such a degree that the muscle could be reached by local application only. This is of great interest in connection with circulatory obstruction in those severely gassed with chlorine. *Hill* found that bromine vapor in a 1:1000 concentration killed the mucous membrane of the trachea so that it might be stripped off by violence of the respiratory effort and be drawn into the larger bronchi, forming a tree-like cast which suffocated the animal. In general, bromine resembles chlorine in its action, but is much more irritating to the conjunctiva and the mucosa of the upper respiratory tract, while there is reason for believing that the pulmonary changes are not quite as marked. If used in warfare as a shell gas the well known cutaneous lesions would be an important part of the pathologic complex.

BROMIDES OF BENZYL, XYLYL and TOLUYL, BROMACETONE, BROMACETIC ETHER, BROMINATED-ETHYL-METHYL-KETONE; and other bromine compounds are used primarily for their lacrimatory effect. The lacrimatory gases are usually liquids at ordinary temperatures and are scattered from shells and hand grenades. The heat of explosion probably suffices to vaporize the liquid as the boiling points of most of these substances range between 110° and 130° *(Filippini).* Concentrations of some of the bromine compounds as low as one part in several millions are said by *Hill* to render men ineffective through lacrimation and photophobia. There are several articles dealing with the lesions produced by unidentified members of this group, but this is otherwise an unworked field. *Tremolières* and *Loew* report upon five soldiers gassed with shells which gave off a heavy, acrid, suffocating yellowish smoke. They felt a severe smarting compelling them to close their eyes, and sharp pain in the throat with violent cough. They felt stupefied and two lost consciousness. In the open air, they revived but continued to have constant lacrimation and photophobia. After several hours sight was obscured and they believed themselves blind. Three had watery greenish vomitus. When seen about thirty-six hours after gassing there was intense congestion of bulbar and palpebral conjunctivae, constant lacrimation and a marked opacity of the cornea so that fingers could be counted only with great difficulty. Purulent bronchitis and bronchopneumonia developed. There was constant cough and the greenish-yellow purulent sputum was often blood streaked. All suffered profound psychical and physical depression. The blood count showed the red cells moderately reduced in number, the leucocytes increased. There were some nucleated reds and coagulation was rapid. At no time were there albumin, sugar or bile pigments in the urine. These patients all recovered, the lung signs clearing up in ten days to three weeks and eventually the corneal opacity likewise disappeared, leaving normal vision. The authors note the reduction of the red blood cells without hemoglobinuria or hemolytic icterus as an interesting feature of these cases. *Agasse-Lafont* and *Roux* report another group of cases gassed by an unidentified lacrimatory gas. All of the five men under observation had persistent vomiting after each meal for several days and then developed all the symptoms of gastric erosion or ulcer. One vomited blood on two occasions. Another had melena and the erosion seemed to be in the duodenum. Gastroenterostomy was done in this case and all symptoms subsided. These case-reports suggest vascular or hemic changes similar to those found in phosgene gassing.

The LACRIMATORS were used alone chiefly in hand grenades, or in shell as a preliminary gas attack followed by shell containing more lethal gases. They were undoubtedly often used with phosgene or mustard gas; ethyldichlorarsine was used in a 50 to 50 per cent combination with dichlormethylether. This shell is said to have produced early sneezing, with later development of symptoms resembling those caused by mustard gas. The effects of xylyl, toluyl and benzyl bromides upon the eyes are said to have been almost instantaneous. Even when diluted 1:1,000,000 of air, the lacrimation produced is so marked that the affected men can not keep their eyes open. In stronger concentrations the effect upon the eyes is most extreme. The lacrimation usually ceases as soon as the men get into pure air, and apparently produces no lasting effects upon the eyes.

CARBON MONOXIDE.—CO. Density, 0.9678. Like nitrous fumes, carbon monoxide was thought by many to have been one of the gases used in the early attacks. Its lightness and the fact that it can be liquefied only by extremes of temperature and pressure make it entirely unsuited for use either as a cloud or shell gas. Its importance, in warfare, is due to its production in enormous quantities as a detonation gas. Readily diffused in the open, it becomes exceedingly dangerous when encountered in military mining. It can be readily detected, even in minute quantity, by the use of mice or canary birds, which are susceptible to about 0.05 to 0.06 per cent. Breathing of otherwise normal air containing 0.2 per cent of CO for several hours will usually cause death and 0.1 per cent may be fatal through cumulative action. Basing his report upon cases due to carbon monoxide gassing in military mines *Sundell* gives a very good description of the clinical picture. The premonitory symptoms are heaviness and loss of power in the limbs and giddiness or light-headedness. The loss of power of the extremities may be so marked that the victims are unable to escape although conscious that they are being overcome, or they may fall from the ladders in trying to climb out of the mine. He notes that these men usually show pallor rather than the classical pink color. Vomiting is an almost constant symptom and headache usually comes on when the men are brought out to the fresh air. In the nonfatal cases this is a very persistent symptom. At autopsy the chief, and often the sole, lesions are punctate cerebral hemorrhages sometimes with ecchymoses in the meninges. Through this finding, the pathology of carbon monoxide poisoning makes contact with that of shell shock, the occurrence of similar hemorrhages in shell shock having raised the question of a common etiology. This problem has been investigated by *Mott* and others. Ulcer of the stomach may also follow carbon monoxide poisoning. In chronic cases of this poisoning a compensatory polycythemia may occur. The treatment of the acute cases consists of artificial respiration, use of pulmotor and oxygen, venesection, stimulants, infusion of normal salt solution, catharsis, and sedatives.

CHLORINE.—Chlorine has a density of 2.450, is liquid at ordinary temperatures under relatively low pressure and is highly irrespirable. It is therefore well suited to use as a cloud or drift gas. *Klotz* found that a concentration as low as 1 part in 10,000 would produce acute poisoning in small animals. *Filippini* gives .05 per cent as a fatal concentration while one of .4 to .6 per cent produces speedy death. In experimental animals death may be produced within one to two minutes with higher percentages.

The symptomatology and pathology of chlorine gassing depend entirely upon the concentration of the gas and the duration of exposure to it. All cases show from the first the most intense irritation of the respiratory mucous membranes with incessant coughing. Those most severely affected die in the trenches within a few minutes, with or without hemoptysis, and when found have a faint greenish yellow appearance like that of asphyxia pallida (*Bradford* and *Elliott*). The literature affords no record of postmortem findings in these immediately fatal cases. In dogs similarly poisoned, the peripheral vessels do not bleed at autopsy and the lungs are found to be shrunken, dry, bloodless, and friable. Men who survive the attack for a few hours develop the most intense acute pulmonary edema with extreme cyanosis, dyspnea and very abundant frothy expectoration, often blood tinged. Most of the deaths occur in this stage. Autopsies of cases dying during this asphyxial stage show (*Black*, *Glenny* and *McNee*, *Henry*, and others) a well marked inflammation of the pharynx and larynx without membrane formation, intense congestion and edema of the trachea and larger bronchi, and a most extraordinary edema of the lungs such that the patient has literally drowned in his own body fluids. Subpleural hemorrhages are practically always present, evidence of the essentially asphyxiative character of the death. Subepicardial and subendocardial hemorrhages may also be present. Intervesicular emphysema is common and mediastinal emphysema by no means rare. In 7 per cent of the cases (*Sisto*), there is a subcutaneous emphysema appearing at the base of the neck and spreading over the anterior surface of the thorax, reaching eventually to the abdomen and scrotum. The heart is dilated, particularly on the right side. All abdominal organs show marked passive congestion. The stomach in all cases shows a marked catarrh and in most cases submucous hemorrhages.

As the intense edema disappears, the frothy sputum gradually becomes more purulent and a severe mucopurulent bronchitis develops. In this stage the damaged lung tissue is especially open to bacterial invasion, and pulmonary gangrene or pneumonia may terminate the picture. Those who have been severely gassed with chlorine, recover but slowly and for months are dyspneic and cyanotic on slight exertion. Just what the reparative process may be in these cases is not yet known but it seems probable that there is marked increase in the fibrous connective tissue of the lung and that the more severe cases undergo to some extent an obliterative bronchiolitis.

As the most striking feature, both of the symptomatology and of the gross pathology of chlorine gassing, the pulmonary edema has aroused much interest. Its appearance is so rapid that it scarcely seems possible that it could be purely inflammatory in character. According to *Hill,* the exudation follows directly upon, and as a result of, the injury to the surface epithelium and underlying capillaries and he cites experimental evidence in support of his belief. *Schäfer,* on the contrary, by a series of elaborate studies on cats, rabbits and dogs came to the conclusion that chlorine produces its fatal results by causing obstruction of the pulmonary vessels, amounting in some cases to complete stasis. He also called attention to the vicious circle between edema and vascular obstruction.

This conclusion of *Schäfer's* has been supported and explained by observations upon the blood and circulatory changes in chlorine gassing, which, taken as a whole, represent the most important advance that has been made in the pathology of gassing. It has been repeatedly noted that the blood of chlorine gassed patients coagulates with great rapidity. So marked is this change that therapeutic blood-letting is oftentimes a matter of much difficulty. The dark colored, thick, viscid blood flowing sluggishly from even large veins is frequently described. Pulmonary thromboses and infarction are also noted in the earlier autopsy reports but no great stress is laid upon their importance, yet thromboses elsewhere in the body are mentioned in case reports with significant frequency. For instance: *Giroux* describes a case of hemiplegia consequent to chlorine gassing which he attributes to the thrombosing action of chlorine; *Sisto* notes thrombosis of a brachial artery; *Bradford* and *Elliott* record three cases with vascular obstruction in the lower extremities, with progressive loss of the arterial pulse, coldness and lividity of the limb and threatened gangrene; *Kramer's* case showed pulmonary and coronary thrombosis together with a parietal thrombus of the left ventricle; *Boldireff* warns that there must be no rubbing of the gassed patient in order to warm him as this is liable to induce embolism. *Pozhariski* finds that among the severe changes, noted in cases dying in the first twelve hours after chlorine gassing, is the marked increase in the coagulability of the blood rendering it thick and unable to circulate freely. He finds white thrombi in many cases and concludes that the blood changes and thrombus formation so embarrass the work of the heart that tissue asphyxia results. He further states that embolism and infarction are to be expected among the complications.

Hake investigated the direct action of chlorine upon the blood *in vitro*, but the conditions of his work were not such as to throw light upon the factors of coagulability. He did find, however, that the characteristic dark bands of the oxyhemoglobin absorption spectrum, as obtained in dilute blood, are discharged by adding chlorine water drop by drop and that if chlorine gas is allowed to bubble through dilute blood, the iron of the hemoglobin, at least in part, passes into solution in the colorless filtrate and can be there demonstrated by the usual tests. He calls attention to this permanent destruction of the hemoglobin as a possible explanation of the immediately fatal cases of chlorine gassing, since this change if it takes place in the human body would be more serious even than the more or less temporary fixations of carbon monoxide and cyanogen with hemoglobin.

The recently published work of *Klotz* is an important contribution to the study of the blood changes in chlorine gassing. He finds that in severely and fatally gassed animals there is microscopical evidence of coagulation within the dilated capillaries. While this may be the result of the abstraction of fluid, as may also be the increased viscosity of the blood, it seems more probable that the local and direct effect of the chlorine hastens coagulation for he shows that human blood in an atmosphere of 1-1000 chlorine coagulates in about 15 seconds and more rapidly in stronger concentrations. He does not, however, assign this as the sole reason for the acute deaths. "It would appear that the acute deaths of the experimental animals were the direct result of obstruction of the pulmonary circulation and that the presence of the pulmonary edema was a factor in this regard." If the individual lives somewhat longer, the fatal result is more particularly associated with the edema.

It will thus be seen that the most important action of chlorine is, perhaps, its power to lower the coagulation time of the blood. If further experimental work supports this view, it will completely alter all former conceptions of the pathology of chlorine gassing. As a working hypothesis, it explains the immediate deaths; the dry and almost bloodless condition of the lungs in animals gassed with rather high concentrations; the initiation of the vicious circle which includes pulmonary stasis, pulmonary edema, concentration of the blood, and cardiac dilatation; and the thrombosis, infarction, embolism and multiple hemorrhages which are part of the clinical picture.

The changes in the cellular elements of the blood are apparently not important. The erythrocyte count, as reported, is usually about normal, although the concentration of the blood by the extreme pulmonary edema must be remembered. Evidence of a slight hemolytic icterus has been given in a few case reports, but hemolysis does not play any great part. *Heitz* quotes *Below* that the hemoglobin reading of fifteen subjects examined on the eighth to eleventh day averaged 100 per cent. The white cells in this same series of cases ranged from 7,000 to 10,000. *Miller* finds that a case which has been gassed sufficiently severely to produce symptoms lasting for some time shows a more or less marked relative lymphocytosis which takes some time to develop, three to four months, at least. This he attributes to chronic inflammatory changes in the lung.

The gastrointestinal lesions in chlorine gassing are also important. Acute epigastric pain, with vomiting, oftentimes bloody, is very frequently one of the early manifestations. Altered blood may be vomited for several days following the gas attack and those who have been at all seriously affected usually show anorexia and intolerance of food. *Leoper, Peytel* and *Sabadini* describe cases which had unmistakable signs of a severe erosive gastritis, eventually relieved by bicarbonate of soda and a milk diet. Reference has already been made to the changes found postmortem in the stomach; congestion, petechial hemorrhages, patches of bloody suffusion and in some cases ulcerations. *Bradford* and *Elliott* found the stomach full of blood in two out of sixteen autopsies. Similar but less marked changes have been described for the duodenum. *Sergent* and *Agnel* attribute the gastric changes to local caustic action from swallowing the gas. They are more probably asphyxiative, embolic or thrombotic, or arise from the digestion of small hemorrhagic areas in the gastric mucosa. An increasing number of cases of gastric ulcer following gassing with the asphyxiating gases is being reported in the recent literature.

In regard to changes in the central nervous system *Neiding* states that of 274 cases of drift gas poisoning (probably chlorine, but possibly chlorine combined with phosgene) more than 50 per cent presented objective nervous manifestations. The headache and feeling of extreme fatigue are considered by *Bradford* and *Elliott* as signs of toxic lesions of the central nervous system, but they found no gross changes in the brain at autopsy. Miliary hemorrhages are described by several, but they seem to be a much less constant finding in chlorine than in phosgene poisoning.

Chlorine gassing does not produce characteristic parenchymatous changes in either liver or kidneys. Surprisingly few cases have shown albuminuria. After the first week the percentage is higher, but this is doubtless to be attributed to the advent of pulmonary infections. *Bradford* and *Elliott* found that in all men dying in the second week the kidneys showed the changes of a moderate acute parenchymatous nephritis, yet none of them had had edema, and only one uremic symptoms; and the authors emphasize the usual absence of albumin and casts in their gassed cases.

Sergent and *Agnel* suggest that the feeling of general weakness, the great fatigue, the hypotension and fall of temperature call to mind the phenomena of suprarenal insufficiency. *Voivenal* and *Martin* insist that gassed cases show a suprarenalitis with insufficiency. There is, however, no gross or microscopical evidence of structural changes in the adrenal in cases known to be due to uncomplicated chlorine poisoning.

Treatment.—The treatment for chlorine poisoning is essentially the same as for phosgene, with the addition of ammonia inhalations.

Chloropicrin, Acrolein, Methylchlorosulphate and probably other organic compounds (*Vaughan*, *Filippini*) have been used for their lethal effect. The literature as yet gives no detailed discussion of their pathology except for chloropicrin (*Winternitz* and *Underhill*). In general, they are necrotizing irritants to conjunctival and respiratory mucosæ and produce an asphyxial death through pulmonary edema and congestion. The same treatment is recommended for cases gassed with chloropicrin, as for phosgene and chlorine; early blood-letting, saline infusions, and oxygen; and a restoration of the normal concentration of the blood.

Cyanogen and Cyanides: It was expected that cyanogen and its derivatives would play an important part in military gassing. As a matter of fact, these expectations were disappointed, because of difficulties attending the use of hydrocyanic acid and its instability under the conditions of concussion and heat, as well as for the fact that more poisonous gases like phosgene were more easily available. Allyl-iso-thiocyanate (mustard oil) is said to have been used to some extent, but no details are available. It is probable that there was a confusion of this substance with mustard gas (dichlorethylsulphide) in the minds of some writers.

Dichlormethylether ($C_2H_4Cl_2O$) was used in Yellow and Green Cross Shells as a solvent and vaporizer for dichlorethylsulphide, and also in combination with ethyldichlorarsine. It is an irritant to skin, conjunctiva and mucous membranes; its action is very similar to that of mustard gas, although weaker. Treatment is similar.

Monochlormethylchloroformate (Palite), and Trichlormethylchloroformate (Diphosgene, Superpalite or Surpalite) are among the most powerful respiratory irritants known. Their action is similar, but the diphosgene is the more powerful and it, therefore, came to be used in place of the former. It diffuses quickly, and a dilution of 1:1,000,000 is toxic if breathed for some time. In stronger concentrations a few whiffs may cause death through spasm of the larynx. It causes little local irritation, and in diluted form may be breathed for some time without symptoms beyond slight conjunctival smarting and pharyngeal irritation. As in the case of phosgene poisoning the toxic action in slightly gassed cases may be delayed, particularly if the gassed individual is subjected to exhausting exercise after the gassing. The chief action is upon the parenchyma of the lung, with the production of an intense congestion and edema. The symptoms vary in degree proportionately to the exposure. The slightly gassed cases may show only slight cough, nausea, vomiting, headache, thoracic soreness or constriction, epigastric pain, dyspnea, and general weakness. The more severe cases are very dyspneic, cyanotic, with cough, frothy or bloody sputum, general venous congestion, and marked weakness. The physical signs are those of a pulmonary edema, with dilatation of the right heart and increased pressure in the pulmonary artery. The most severe cases show marked collapse, low blood pressure, rapid and thready pulse, rapid and shallow respirations, gray color of skin, and progressive cardiac dilatation. Death takes place usually within twenty-four hours from this cause. Recovery may take place after this time, and the edema may clear up after the second or third day. Cardiac dilatation may persist for some time, and such cases may die suddenly from exertion or overeating.

The pathologic findings are congestion and edema of the lungs, with capillary hemorrhages, general venous congestion, and dilatation of the heart.

The treatment is the same as for phosgene poisoning; rest, venesection, oxygen, cardiac stimulation, and isotonic saline infusions.

Nitrous Fumes.—N_2O_3, nitrous anhydride, density 2.63; and NO_2, nitrogen peroxide, density 1.57. In the first few months of the gas attacks many writers believed, probably incorrectly, that the oxides of nitrogen were being used. There was little to support this view and nitrogen compounds are too valuable to be used in this manner, but the oxides are nevertheless important as detonation gases from many of the high explosives now used. This hazard is also met in civil life, as described by *Watt* and *Irvine* for the Transvaal mines, where burning blasting gelatin produces these fumes. One of the most characteristic features of nitrogen peroxide poisoning is its delayed action. *Hill* calls attention to the fact that firemen exposed to the fumes of nitric acid are unaffected at the time but develop a fatal inflammation of the lungs during the next twelve hours. Gassing with nitrous oxides as it occurs on board ship is discussed by *Ohnesorg* in a review of the work of *Esch*. There is usually a little headache, cough and tightness of the chest which soon passes off. Then in six to eight hours there is dyspnea, cough, bloody serous expectoration, and death from asphyxia and heart failure occurs in about forty-eight hours. At autopsy there are found pulmonary congestion, edema, and marked inflammation of the mucosa of the trachea and larger bronchi. A bronchiolitis obliterans may develop in the lungs of those not fatally gassed.

Phosgene. $COCl_2$, Carbonyl-chloride.—Phosgene is a liquid which boils at 8.2°, giving off a colorless gas which is exceedingly suffocating and irritative. The density of the gas is 3.49 as compared to air. It is used both as a shell gas and a drift gas, in the latter case usually mixed with nine parts of chlorine. Pure phosgene can not be used in cylinders because it does not come out satisfactorily. It is used in mixtures of 25 per cent to 50 per cent with other gases.

Phosgene poisoning closely resembles chlorine poisoning but is considered by all as being more serious. *Vaughan* says that phosgene is twenty-four times as effective as chlorine, and *Filippini* gives 0.25 per cent as a concentration which is rapidly fatal. The toxic action has been attributed to carbon monoxide produced by decomposition in the presence of water according to the formula,—

$$2\ COCl_2 + H_2O = 2\ CO + 4\ HCl + 2\ O.$$

but this is probably not the true explanation.

The pre-war literature dealing with the lesions of phosgene poisoning has been reviewed by *Filippini*. He cites the cases of *Müller* and of *Roos* as reported by *Bilancioni*. One of *Müller's* cases came to autopsy showing a marked dilatation of all the chambers of the heart. The five cases of *Roos* showed in life, cough, cardiac dilatation, weak pulse, marked cyanosis, polycythemia, marked concentration of the blood, marked leucocytosis with lymphopenia, and albumin, indican, urobilin and casts in the urine. Autopsy of the two cases which died showed focal pneumonia, subpleural hemorrhages, acute bronchitis, multiple thromboses of the pulmonary arteries, fatty degeneration of liver and spleen, and minute thromboses of cerebral and intestinal vessels.

In experimental phosgene gassing of rabbits and cats *Bilancioni* found the most severe contact lesions, the mucosa of larynx, trachea and larger bronchi being in a state of necrobiosis and desquamating in large strips. There was marked pulmonary edema and congestion with thromboses and hemorrhagic infarctions. In some cases the intrinsic laryngeal muscles showed fragmentation, which he thinks may have been due to, or favored by, the convulsive opening and closing of the larynx. The laryngeal lesions, particularly the hemorrhages into the submucosa, and the extreme pulmonary edema he considers the most important features.

Similar pulmonary lesions are found in the human cases, and the occurrence of thromboses is also repeatedly mentioned. The Italian writers emphasize the frequency of thrombosis of mesenteric vessels resulting in some cases in a diffuse necrotic enteritis and localized peritonitis. Punctiform hemorrhages in the brain are also a frequent finding. These are considered by *Mott* as of embolic origin, possibly due to pigment granules of altered hemoglobin. In the brains of two cases of drift gas poisoning he found the white matter peppered with innumerable hemorrhages, each about the size of a pin head. These were microscopically like those of carbon monoxide poisoning except that the hemoglobin appeared to have been largely converted into chocolate colored granules, a change which he thinks may have been due to the action of hydrochloric acid, liberated from the phosgene, in converting the hemoglobin into acid hematin.

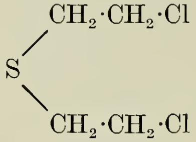
As the strength of the phosgene concentration in the German shell increased, the gas cloud produced became progressively more toxic so that according to *Auld* a couple of breaths of the poisoned air became enough to kill a man. The lighter cases of phosgene gassing in the army showed severe and painful coughing, bronchitis, nausea, retching and vomiting. One important feature was the so-called "delayed" case, in that many men who thought that they were only slightly gassed, became ill, or died, several hours or days later, particularly if they had taken any muscular exercise immediately after exposure to the gassing. Death in these cases seemed to be due to acute cardiac dilatation resulting from fatigue after the gassing. The importance of rest in the case of mild phosgene gassing was afterwards emphasized in the treatment of these cases so that the delayed cases became greatly reduced in number. As far as prognosis is concerned, the degree of cyanosis and concentration of the blood are important guides to controlling the treatment which consists essentially of attempts to relieve the respiratory and circulatory embarrassment. Early bleeding, followed by intravenous infusions of isotonic salt solutions have been recommended for the treatment of phosgene, chloropicrin, and chlorine poisoning. (*Winternitz* and *Underhill.*)

PHOSPHINE.—PH_3, density 1.214, has been used in warfare. The lethal concentration is given as 0.025 per cent. It kills directly by virtue of its own toxicity.

SULPHUR DIOXIDE.—SO_2. Density, 2.21. Sulphur dioxide is easily liquefied by cold and pressure and has been used, according to *Lung,* in hand grenades, filled with the liquid and provided with a small bursting charge to scatter the contents when thrown. It is a respiratory irritant and in sufficient concentration produces pulmonary lesions and asphyxia. It is not effective unless comparatively concentrated and apparently has not been much used as it is mentioned by but a few authors. SULPHUR TRIOXIDE. SO_3. This was used in shells and grenades to produce finely suspended particles that remain in the air for long periods of time as "smoke," uniting with the moisture of the air to produce sulphuric acid. HYDROSULPHURIC ACID. H_2S. Colorless gas of characteristic odor. Density compared to air, 1.191. Gaseous at all ordinary temperatures and pressures. Other than reports of its use, little information in regard to poisoning with hydrosulphuric acid gas has appeared in the war literature. *Filippini* says that death may follow its inhalation at a concentration of but .07-.08 per cent, if continued for some time, and that 1.5-2.0 per cent is rapidly fatal.

Physical and Chemical Properties of Mustard Gas

MUSTARD GAS (BETA-BETA-DICHLORETHYLSULPHIDE, THIODIGLYCOLCHLORIDE),



perhaps the most important gas used in the war by the Germans, as it gave them their most important gas victories, was first made by *Victor Meyer* in 1886. He described it as a heavy, oily fluid sinking below water and not miscible with it, of neutral reaction, having a faint, sweetish, ethereal odor but slightly suggestive of the sulphur compounds, and with a boiling point of 217° C. The pure substance furnished us by Major Gomberg was a clear, colorless, heavy oily fluid, with a very faint cress-like or mustard odor, more like that of the freshly bruised plant than of prepared mustard. The boiling point was 217° C. Samples of this preparation over a year old are unchanged. All other samples of dichlorethylsulphide, that we have seen, were more or less impure, having a slight or marked yellowish or brownish color and a more decided odor. These impure samples have become browner and more odorous. The pure substance causes no staining of the tissues, the impure ones may stain the tissues a bright yellow. The Germans used mustard gas in their Yellow Cross and Green Cross shells, in percentages varying between 60 and 80, in combination with carbon tetrachloride, dichlormethylether, chloroform and chlorobenzene, the object of these substances probably being to act as vaporizers or lower the freezing point. Dichlormethylether, in addition, is also an irritant to the skin and mucous membranes. Carbon tetrachloride is the most satisfactory solvent of mustard gas, and being volatile leaves a residue of the latter behind. Mustard gas was first used effectively by the Germans at Ypres, July 12 and 13, 1917, and from that time to the end of the war it proved to be their most effective war weapon. The facts that it is toxic in concentrations so slight that it may not be detected by its odor, that it penetrates clothing and affects the skin particularly in sweaty areas (axillæ, genitalia, etc.), that it is painless in its action upon the skin, that its action is delayed, and that it is remarkably persistent have made it above all others, the form of poison gas most dreaded by the soldier, although not to be compared in fatal toxicity to chlorine, phosgene or diphosgene. Against these, however, the gas masks offer protection, as they also do against the respiratory action of mustard gas. But the insidious action of the latter upon human skin, and the difficulty of protection therefrom, give this gas an importance of a special kind. Perhaps no other gas so served to break the morale as this one. Its disabling or neutralization qualities far exceed its killing powers. Its name of "mustard" is a soldier's term, from the odor of the impure substance used in gas shell. By the French it is called *yperite*, and by the Italians, *yprite*.

Because of its persistence, its slowness of vaporization, its re-solution on wet surfaces, and its ready solution in fatty substances, this gas is particularly dangerous. Casualties may be produced hours or even days afterwards in areas affected by mustard gas shell. Clothing, weapons and other articles exposed to it may produce severe lesions some time afterwards, even when no odor is perceptible.

It may be destroyed by chlorine, most conveniently applied in the form of bleaching powder, or other actively chlorinating compounds. In the presence of water dichlorethylsulphide is gradually hydrolyzed to hydrochloric acid and dihydroxyethylsulphide. As the latter substance is inert, the injurious action of mustard gas has been ascribed to the effects of hydrochloric acid. As will be shown later, the toxic action of mustard gas is probably not as simple as this explanation would indicate.

Homologues of Dichlorethylsulphide, and Related Bodies

The Beta-Beta isomer of Dichlorethylsulphide is toxic; the Alpha-Alpha isomer is not.

Monochlorethylsulphide.—*Victor Meyer* found that the toxic properties of this substance were much less marked in intensity than those of the dichlorethylsulphide. Dichlorpropylsulphide.—The alpha and beta isomers have about the same action, but are very much less toxic than dichlorethylsulphide. Dichlorbutylsulphide has a toxic action estimated to be only about one-one-hundredth that of dichlorethylsulphide. Tetrachlordipropylsulphide, dichlormethylsulphide, tetrachlormethylsulphide, perchlormethylsulphide, tetrachlorethylsulphide, hexachlorethylsulphide, monochlorethylmethylsulphide, dibromethylsulphide and diiodoethylsulphide are all less toxic than mustard gas and hence of less value in military gassing.

When this research was first begun, there was no literature available as to the pathologic effects produced by dichlorethylsulphide beyond Victor Meyer's first descriptions. During the progress of the work, the articles that appeared, as will be shown by the reviews of the literature, were chiefly superficial clinical and gross pathologic observations. The field explored in this research was therefore a virgin field and in our eighteen months' work we feel that we have solved the major problems of the pathology of dichlorethylsulphide poisoning. As far as the cutaneous, ocular, respiratory and systemic pathology are concerned, we feel that the work is complete. But one point remains, to our mind, not completely settled and that is the mode of action of the poison in the causation of death following subcutaneous and intravenous injections.

Confirmation of some of our work has already appeared in some recent papers published by other investigators.

CHAPTER II

THE CUTANEOUS LESIONS PRODUCED BY MUSTARD GAS (DICHLORETHYLSULPHIDE)

Victor Meyer,[1] the discoverer, in 1886, of dichlorethylsulphide, at once recognized the specific toxic properties of the substance from the fact that a laboratory worker engaged in making it, suffered from a severe skin eruption and a transitory conjunctivitis. As Meyer himself was not affected by exposure to the substance, he concluded that individual susceptibility to it must vary greatly. Animal experiments were carried out as follows: Two medium-sized rabbits were confined three to four hours in a closed cage ventilated by a moderately strong current of air passing through a glass tube containing strips of blotting paper saturated with thiodiglycolchloride (dichlorethylsulphide). The animals became restless, rubbed their noses frequently with their feet. The nose and conjunctiva became reddened, and the eyes moist. Perspiration appeared to be increased. On the following day both eyes were severely inflamed, the lids glued together with purulent secretion. Marked snuffles developed, the lobes of the ears were much swollen, and the auditory passages showed a purulent inflammation. On the evening of the third day the animals died of a severe pneumonia diffused throughout both lungs. A large rabbit that had inhaled the vapor of the substance for a few hours through a tracheal fistula, without exposure of the surface of the body to these vapors, died of a widespread pneumonia on the evening of the same day, before other symptoms had appeared.

In rabbits in which the unbroken skin of the tip of the ear had been touched with a fine brush containing a small amount of the chloride the site of the application showed no direct effects, but the entire ear became markedly swollen, and in one case a profuse purulent inflammation arose from the bottom of the auditory passage. In this case, the material could not have accidentally entered the auditory canal owing to the small amount used and the fact that it was applied to the outer surface of the ear. In one case in which the skin was scraped by the removal of the hair from the ear tip, the chloride applied by means of the brush caused an especially severe suppuration at this point, and also a marked swelling of the whole ear and inflammation of the eyes.

After subcutaneous injection of about two drops of the chloride into the back of a rabbit there developed inflammation of both eyes, very severe snuffles, and on the third day death from pneumonia. At the point of injection no effects were apparent.

The experiments were discontinued because of similar unpleasant effects upon those engaged in the investigation. Meyer concluded that the most severe action of the chloride develops only after its entrance into the blood. Preliminary experiments with the glycol and the sulphide showed these to be nonpoisonous.

In 1887, *Meyer*[2] stated that experimental animals surviving after application of thiodiglycolchloride (dichlorethylsulphide) to the ear, showed a persistent profuse suppuration and complete necrosis and falling off of the ear after a few weeks. Because of the marked toxic action of the dichlorethylsulphide, physiologic tests were made of the monochlorethylsulphide. This was found to possess poisonous properties like those of the dichlorethylsulphide, but less marked in intensity. In the comparison of these two substances and ethylsulphide, the chlorine-free sulphide was found to be harmless. The toxicity of the mono- and dichlorethylsulphides, therefore, depends entirely upon the chlorine content.

From 1887 up to 1917, the poisonous nature of dichlorethylsulphide seems to have attracted little attention in either chemical or medical literature. Since its use as a poison gas in warfare, the name "mustard gas" has been almost universally applied to it because of the faint mustard-like odor; and from the war literature and war reports further knowledge of its toxic action has been gained.

The symptoms of mustard gassing are described in the British Army Reports as follows: Initial tendency to sneeze without irritation of eyes or lacrimation, with a gradually increasing nose and throat irritation, followed after about twelve hours by a free discharge of mucus from nostrils, painful irritation and inflammation of eyes, and occasionally vomiting. Many men had pain in forehead and stomach. Small blisters may form on face and neck; the skin between thighs is occasionally red, sore and sometimes blistered. Contact with fragments of shells and with the earth near shell holes may cause blistering through the clothes. None of these lesions manifests itself at once; they develop after several hours. The pain in the eyes may lessen after twenty-four hours, although acute inflammation may persist several days. In severe cases bronchitis and pneumonia may develop after thirty-six to forty-eight hours. There are usually no deaths under twenty-four hours. Prolonged exposure to small concentrations of the gas causes laryngitis and loss of voice, sufficient to put men out of action. Of the men affected practically all have conjunctivitis, about 95 per cent have throat and lungs affected, and about 70 per cent show skin burns. After six weeks the skin lesions are usually healed. The eye, pulmonary, and cardiac conditions recover more slowly.

Giraud,[3] in November, 1917, describes the early symptoms of mustard-gas poisoning, dividing them into three groups: eye lesions, respiratory tract lesions, and burns. All of these develop slowly, but the time of appearance varies for each lesion. The eye symptoms appear first, within six to twelve hours and are fully developed at the end of twenty-four to forty-eight hours. The respiratory affections usually appear at the end of two to four days. The skin lesions fall into two groups, the earlier burns, contemporaneous with the conjunctivitis or preceding it, and later burns. The early burns are the most severe. The later burns appear at the end of four, five, eight, ten or even fifteen days. They are usually without danger. The three groups of lesions may be found singly or associated in the same individual. Giraud also finds that the eye lesions are most common, then follow those of the respiratory tract, and thirdly the burns.

EYE LESIONS.—Conjunctivæ congested, vessels dilated, severe pain at times but usually moderate, moderate lacrimation, vision unimpaired, pupil reflexes normal, marked swelling of eyelids. The less severe cases heal in two to three days.

LESIONS OF THE RESPIRATORY TRACT.—The initial symptom is aphonia which may come on suddenly or be preceded by a few paroxysms of coughing. It is usually complete, lasting three to four days. Tracheitis and bronchitis then develop, the paroxysms of coughing are frequent and painful, closely simulating the cough of pertussis. At the end of two to three days, the patient discharges an abundant mucous or mucopurulent sputum. The affected patients can not breathe except in the erect position, and the majority decline to go to bed. Giraud has not observed hemoptysis. The respiratory affections are most intractable, and frequently relapse without any apparent reason.

SKIN LESIONS.—The early burns appear in twelve hours. These are the severe burns, presenting the appearance of large erythematous patches covered with large bullæ, containing a serous or seropurulent fluid. Occasionally, particularly on the scrotum, the large blisters are replaced by little purulent vesicles surrounding the roots of the hairs. *The pain is commonly quite severe*, and patients presenting burns of this degree are immediately evacuated. The lighter burns are more frequent, are insidious, appear slowly, but are the least serious of the mustard-gas lesions. Often they are unnoticed by the men, and are discovered only by chance. They appear as burns of the first degree in the form of erythematous plaques resembling sunburn. After a time, the central portion desquamates, leaving a slightly weeping surface without any actual blister formation. The burns appear most commonly around the joints of the lower extremities, thighs, genitals, buttocks, neck, and back. They are only exceptionally found upon the uncovered parts.

As to lesions of the digestive tract Giraud considers them exceptional, the frequent vomiting being attributable to efforts at coughing. He considers it probable, however, that lesions of the alimentary tract may be due to ingestion of food tainted by the gas.

All of the lesions observed by him have been purely local. He has only rarely seen signs of general disturbance, acceleration of pulse and fever, which he considers may have been due to other causes than the intoxication. The majority of the patients present an earthy pallor, but this is not surprising in men subjected to the fatigue of a prolonged stay in the first line trenches.

For prophylaxis and treatment he advises the use of a solution of bicarbonate of soda in a strength of thirty parts per thousand. Washing the eyes with the solution he found to be prophylactic against the conjunctivitis. For the burns he employs washing with the bicarbonate solution and a dressing of Vincent's powder (boric acid and calcium hypochlorite). The respiratory lesions he found resistant to treatment, which has been wholly symptomatic.

Teulières,[4] in the same month, November, 1918, describes the action of the gases used in warfare upon the visual apparatus. Under the heading of the "new gas," which he states is composed of carbon tetrachloride and ammoniumbichlorsulphide,* but described by the majority of soldiers as having a mustard odor, colorless, very heavy and impregnating the earth, and which, therefore, must have been dichlorethylsulphide, he says that the ocular lesions produced by it range from simple palpebro-conjunctival reddening up to the most severe burns of the conjunctiva and cornea. Since the gas seems to operate only in the presence of water, he advises against bathing the wounded. The treatment he advises is purely symptomatic.

Mandel and *Gibson*[5] give a brief account of the clinical manifestations and treatment of mustard-gas poisoning, adding nothing to what has been gained from Giraud's article, except the statement that the myocardium, as demonstrated by necropsy, is not damaged. Their summary is as follows:

1. An interval (four to sixteen hours) of freedom from distress exists between the actual gassing and the onset of the symptoms.
2. The cardinal symptoms, conjunctivitis, laryngitis, bronchitis, and skin burns, are all due to the excoriating effect of the gas.
3. The principal complications are early pulmonary edema and relatively late bronchopneumonia.
4. Dry clothing and sleeping quarters may prevent the development of symptoms after slight exposure, and possibly may lessen the severity in those more severely gassed.

Experimental

Haldane[6] states that he has confirmed Meyer's statement that subcutaneous injection of the substance is capable of causing conjunctivitis and death from pneumonia, owing to the absorption of the gas into the circulation.

Kolls and *Gilbert*[7] report that 10 mg. of an alcoholic solution injected into the muscles, and intravenously, produced nothing more than temporary inactivity and loss of appetite, with recovery in one week; 50-100 mg. in alcohol and water emulsion produce convulsions within an hour and death in three hours. *Mice* exposed to the vapor after five minutes became depressed, developed irritation of nostrils and marked dyspnea. Except when high concentrations were used death was delayed two to six days. *Cats* exposed fifteen minutes to a concentration of 1:2000 showed lacrimation and restlessness; after two hours they became wild, kept eyes closed; after twenty hours became dyspneic and died at thirty-six hours. A fifteen-minute exposure to a concentration of 1:10,000 gave similar results; the animal died in four days of pneumonia. In twenty hours photophobia and purulent conjunctivitis developed. *Rabbits* exposed for four hours to less than 1:100,000 concentration closed their eyes toward the end, developed well-marked conjunctivitis at end of twelve hours, and died in two days. After exposure to 1:20,000 concentration conjunctivitis developed in six hours, and was marked in twenty-four; there was marked dyspnea and snuffles after twenty hours.

Raper and *Ball*[8] found that rabbits exposed for five minutes to a concentration of 1:20,000 developed a very slight irritation of the eyes after five minutes; six hours later both eyes were kept closed, and there was a definite conjunctivitis which grew steadily worse with signs of nasal catarrh. When killed after four days there was found an intense congestion of the trachea and some patches of bronchopneumonia. A fifteen-minute exposure caused marked discomfort after ten minutes in the form of a marked irritation of eyes and nose; five hours later conjunctivitis and snuffles had developed. This was worse the following day, and the inflammation of the eyes became purulent. When killed on the fourth day similar changes to the above were found. Thirty-minute exposures produced the same results.

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*Corrected by author in erratum.

Marshall and *Miller*[9] worked with dogs. They found that higher concentrations (38 mg. per liter) caused immediate excitement, irritation of eyes and lacrimation, followed by dulling of cornea and depression. Frequent retching and vomiting was observed. At the end of exposure or shortly afterwards the mucous membranes were inflamed, and, in some cases, the skin on face and bare parts of hind legs became red. There was continued retching and vomiting, nasal discharge and salivation, dyspnea, tracheal rattle, and death in four to ten hours. With lower concentrations there was practically no sign during exposure. In twenty-four hours there developed conjunctivitis, nasal discharge, and tracheal rattle, and animals became depressed. There was no vomiting, as a rule. Death occurred in twenty hours to twelve days.

Kolls and *Gilbert*[10] showed that 1:100 alcoholic solutions act as skin irritants. With increasing dilutions up to 1:1000 the skin is killed, but there is little difficulty in healing. Further dilution produced no irritation. The skin lesions were found to show great individual variations.

Test tubes containing air saturated with mustard-gas vapor applied to the skin caused erythema in twenty-four hours after five minutes' exposure; after ten minutes' exposure erythema was more marked; after twenty minutes' exposure there developed in twenty-four hours a red papular area just short of a blister, with hyperesthesia. When the concentrated vapor is allowed to act on the skin for a short time a vesicle may not be produced, but only a red edematous patch with slight soreness on surface, something like a sunburn (Royal Society War Commission Reports).

One to two drops of a 1:100 solution in alcohol applied to the arm caused varying degrees of itching and blistering. Complete healing took place in seven to eight days, although a scar remained.

Other experimenters[11] find mustard gas to be a blistering agent of great power, producing erythema and blistering the skin as well as causing acute conjunctivitis, tracheitis and bronchitis. The intensity of the action seems to be increased by humidity, although if hands are washed immediately after exposure no lesions are produced. If the skin is touched with a glass rod just moistened with the gas and then wiped with cotton there results in two hours a red patch larger than the area touched. This increases in size, and at the end of four hours may be as large as a sixpence. After twenty to thirty hours a well-marked tense vesicle develops, with erythematous area around vesicle. If the latter is opened under aseptic precautions and infection is avoided, the lesion heals normally, but redness persists for three weeks or more. The whole process is painless.

Subjects exposed in chambers containing 1:10,000 (0.709 grams per M^3) of impure oil, when wearing French respirators, showed after six hours irritation of the skin, vomited and felt ill. On the next day there was marked erythema of the scalp, chest, inside of arms, hands, thighs and genitals. The erythema was more marked on one forearm that had been smeared with vaseline and lanolin. On the arm and on the genitals large blisters were produced.

SUMMARY.—The general effects without protection in animals and in man were found to be conjunctivitis, sore throat, hoarseness, gradual necrosis of mucous membrane of air passages, bronchitis, later purulent in character, leading to bronchopneumonia, which may terminate in death, and more or less widespread burns of skin. These affect chiefly covered parts, but the face and hands may also show burns. The skin lesions develop as follows: Erythema, with some irritation or no pain, followed by blister, accompanied, particularly on the genitals, with much swelling and edema. The erythema is attended by diapedesis of red cells. Even when no blisters are formed, there may be dark purplish patches, the color of which does not disappear on pressure. Later these become pigmented dark-brown.

Pathology

Mackenzie[12] states the most important pathologic changes to be those found in the eyes, skin and respiratory system. In experimental animals there is diffuse clouding of the cornea at once which goes on to exfoliation of the corneal epithelium and to ulceration. The corneal vessels show a marked acute congestion; there is an abundant serous discharge, which later becomes purulent. The skin, where there is no hair, about the lips, nose, genitals, nipples and between toes, shows bright red discolorations.

The upper air passages show patches of intense hemorrhagic redness, in the mouth sometimes to the extent of ulceration, particularly at points of contact with teeth and cheeks. The pharynx, epiglottis and larnyx are reddened. From the upper end of the trachea throughout the entire bronchial tree, the mucosal surface is covered with a thick translucent membrane of a pale yellowish color, which is easily pulled off in large strips. It extends down into the smallest bronchi, forming everywhere a complete lining to the tubes. There is no free fluid or froth in trachea or bronchi, as is constant in other forms of gassing. In the medium and small bronchi the membrane occludes the lumen, causing patches of atelectasis. These may be only 0.5 to 1 cm. in diameter, or may involve a whole lobe, depending upon the size of the occluded bronchi. Such atelectatic areas are dark reddish purple, depressed and nearly airless. Their relation to the plugged bronchi can be easily determined. No pleural effusion noted in animals.

No constant changes were found in other organs. Focal necroses were noted in the liver. These appeared on the surface and on cut section as gray spots, size of pinhead or smaller with a central red point. In three animals punctate hemorrhages were found in the adrenal cortex. In about half of the animals swelling and hyperemia of the mucosa of stomach and duodenum were noted; in one case circumscribed hemorrhagic ulcerations were found near the pylorus. No positive relationship of these findings to the gassing was demonstrated.

Haldane[13] noted the pathologic changes in two cats, one exposed two hours and killed four days afterwards; and the other exposed one and one-half hours and killed nine days after. The first cat showed desquamation of tracheal mucosa and the formation of a plug of leucocytes and red blood cells. Similar lesions, but more severe, were found in the bronchial tree; and the lungs showed leucocyte exudation into alveoli, edema and desquamation of alveolar epithelium, and abscesses. The second cat showed thickening and collapse of the alveolar walls, congestion of the pulmonary vessels, desquamation of nasal epithelium, and inflammation of the skin of the ears.

McNee[14] gives autopsy summary of fatal cases. The points noted were acute inflammation of air passages, desquamation of mucous membrane, and formation of false membrane. To this, infection is added in the form of acute purulent bronchitis with atelectasis and bronchopneumonia. Acute emphysema may be present also. Superficial burns are a prominent feature. Acute hemorrhagic nephritis and edema of lower limbs were noted. In two cases degenerative changes in the central portion of liver lobules and minute hemorrhages in brain were noted.

Fig. 1.—One hour after application of mustard gas. Stage of erythema.

Fig. 2.—Three hours after application. Widening and deepening of the erythematous zone with well-marked edema. Development of secondary paler areola.

McLeod[15] from seven autopsies on men killed in action by the gas, concludes that the danger to life from secondary infection is greater than the toxic action of the gas itself.

Dunn[16] from four cases states that the chief lesions are: 1, severe and lasting damage to bronchi and bronchioles; 2, persistence of edema; 3, severe infection of respiratory tract, bronchopneumonia, and in two cases hemorrhagic exudations.

SUMMARY.—The material given above represents the entire pathologic knowledge of mustard gassing available in the literature at the inception of this research. As is readily seen, this pathology is very superficial and incomplete, being made up almost entirely of rather loose superficial gross descriptions. No detailed gross pathologic observations exist at present; and there is practically no microscopic pathology. If a histologic study of the lesions produced by mustard gas exists in the literature, we have not been able to find it. For this reason, as soon as we heard of the new gas in 1917, our laboratory made efforts to secure the substance for the purpose of experimental pathologic work with the view of determining the exact nature of the tissue lesions. Through the kindness of Professor Moses Gomberg, we were furnished with an ample supply of pure mustard gas. The great majority of our experiments have been carried out with this pure di-

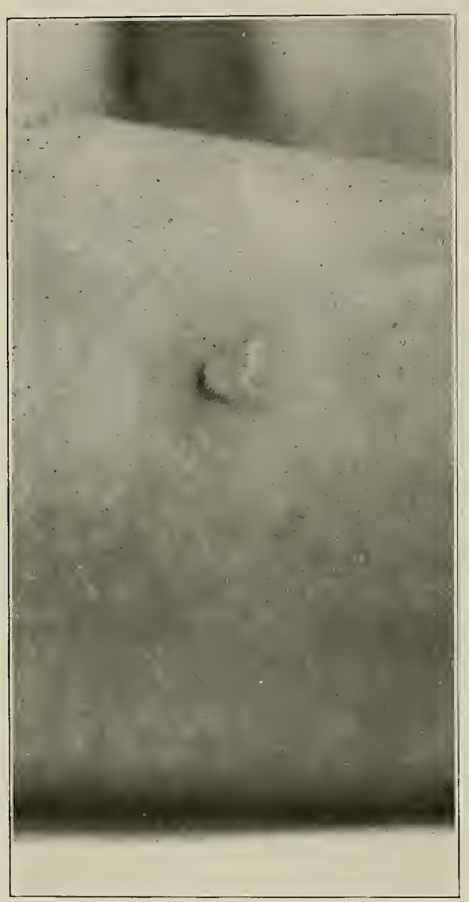

Fig. 3.—Eighteen hours after application. Formation of vesicle on an erythematous base.

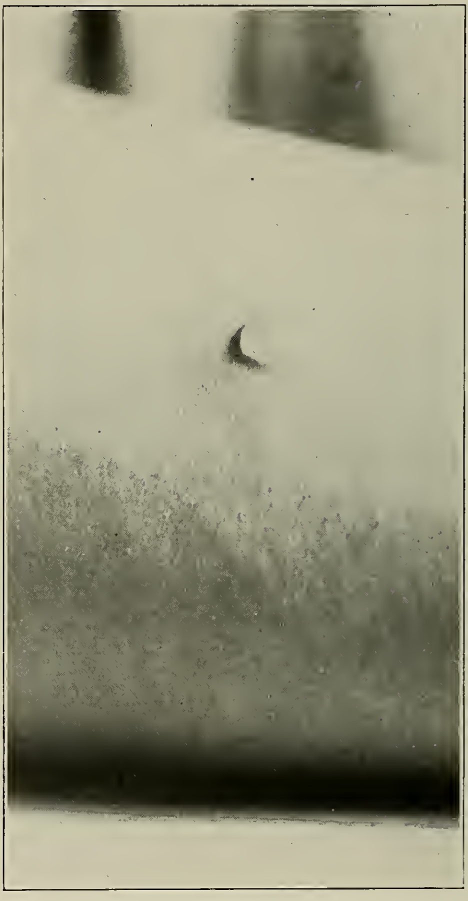

Fig. 4.—Twenty-two hours after application. Vesicle 4 mm. high, tense, fluid content slightly opalescent. Floor of vesicle appears yellowish white, necrotic.

chlorethylsulphide furnished by Doctor Gomberg. It is a clear, colorless, heavy, oily liquid having a boiling point of 217° C. and possessing a faint mustard or water-cress odor.

The present investigation concerns itself solely with the study of the gross and microscopic pathology of the cutaneous lesions, produced in man and animals by the direct application of the liquid or by exposure to the vapor. The human material was obtained from auto-application, amputation material with consent of the patient, accidental chemical laboratory lesions and lesions incurred by workers engaged in the manufacture of dichlorethylsulphide. Through auto-application we have been able to study a complete series of lesions through all stages from inception to healing.

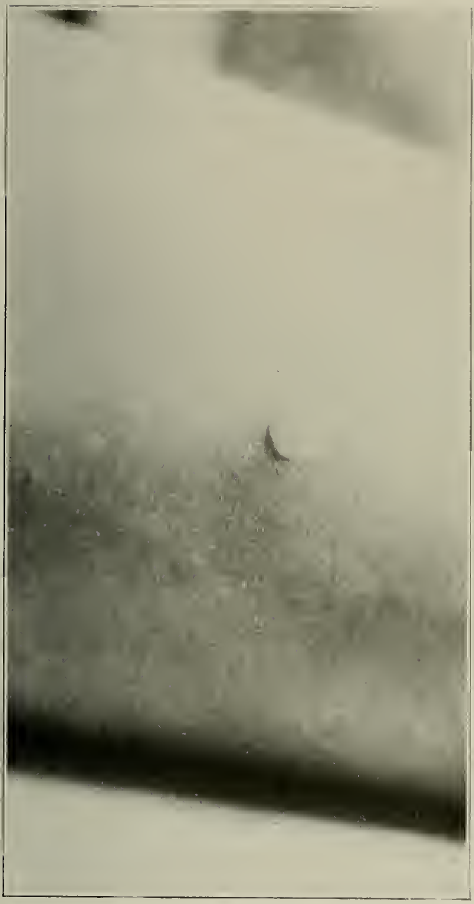

Fig. 5.—Forty-six hours after application. Collapse of vesicle with nearly complete absorption of fluid. Epidermis in fine wrinkles and folds, and of a yellowish brown tint.

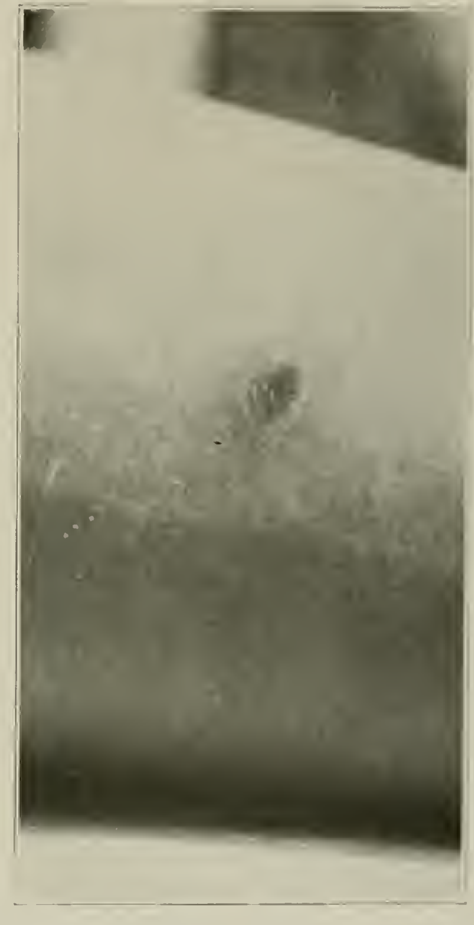

Fig. 6.—Seventy-two hours after application. Beginning eschar formation. Central area bright yellowish brown in color, surrounded by a whitish zone 1-2 mm. in width.

Action of Dichlorethylsulphide on Human Skin

The dichlorethylsulphide was applied by means of a capillary pipette in uniform droplets estimated to be about .0004 c.c. When applied to the skin this drop at once spreads out over an area 3 to 4 mm. in diameter and is completely volatilized, or at least disappears, in one to two minutes, according to atmospheric conditions.

Following is a protocol of the most important stages in the development of the skin lesion produced in this manner. We have found that the rate of production of the lesion and the intensity of the reaction vary over a considerable range in different individuals, notably in a Charcot-joint leg and in a case of malignant disease the development of the vesicle was delayed.

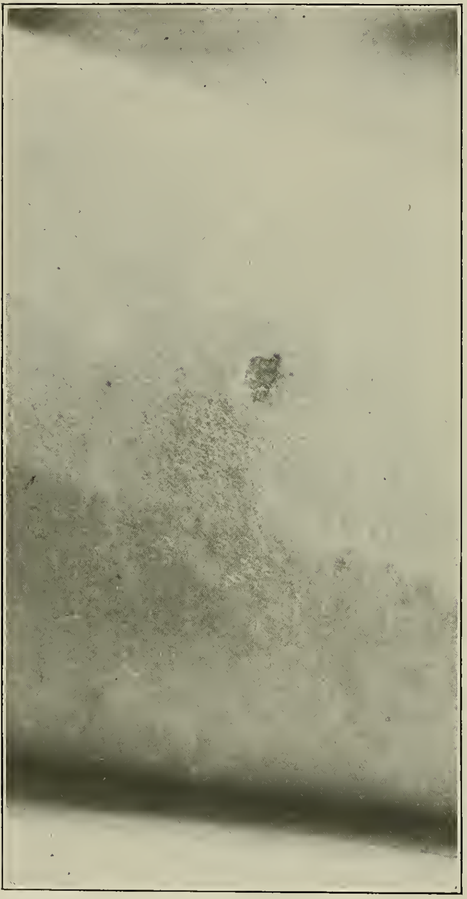

Fig. 7.—Four days after application. Beginning sloughing. Loss of necrotic, wrinkled epidermis. Persistence of white zone and zone of erythema.

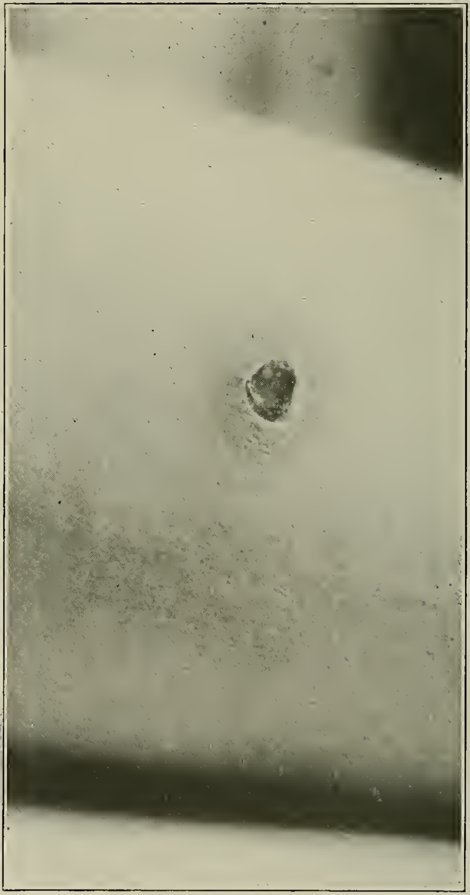

Fig. 8.—Nine days after application. Beginning separation of necrotic base from the peripheral white zone. More marked erythematous zone.

Auto-application to skin of normal individual. March 12, 1918, 2:30 P.M. Standard droplet applied to flexor surface of left forearm. In one minute the liquid completely disappeared giving off a strong mustard odor. There were no subjective symptoms. In about ten minutes there appeared a delicate silvery gray sheen over the surface of the area of application. This was soon followed by a faint flush which gradually deepened and spread until it was about 7 mm. across. Photograph in Fig. 1 was taken one hour after application. At this stage the erythema was influenced by changes of temperature, etc., alternately paling and reddening. Whenever the area became somewhat paler the superficial silvery luster was visible. During the second and third hour a well-marked edema appeared and the erythematous zone became wider and more deeply colored.

Same day, 5:30 P.M. At this time the lesion measured 15 mm. in diameter. It was slightly elevated and had a marginal zone somewhat deeper red than the central portion. Outside of the red zone there was a very faint, barely perceptible zone showing less color than the remainder of the skin. (Fig. 2, photograph three hours after application.) In the next several hours there was no change.

March 13, 1918, 6:30 A.M. Sixteen hours after the application a vesicle began to form. At 8:30 A.M., eighteen hours after the application this was at its height. (Fig. 3.) At this time the lesion measured 25 mm. in diameter. It presented an erythematous base, slightly elevated, and fading gradually into the surrounding skin. Upon the summit of this erythematous base, there rose a tense vesicle 6x9 mm. in area and 3 mm. high. This was filled with a clear pale yellow fluid. Up to this time there had been no subjective symptoms, but with the formation of the vesicle there was slight smarting, increased by pressure.

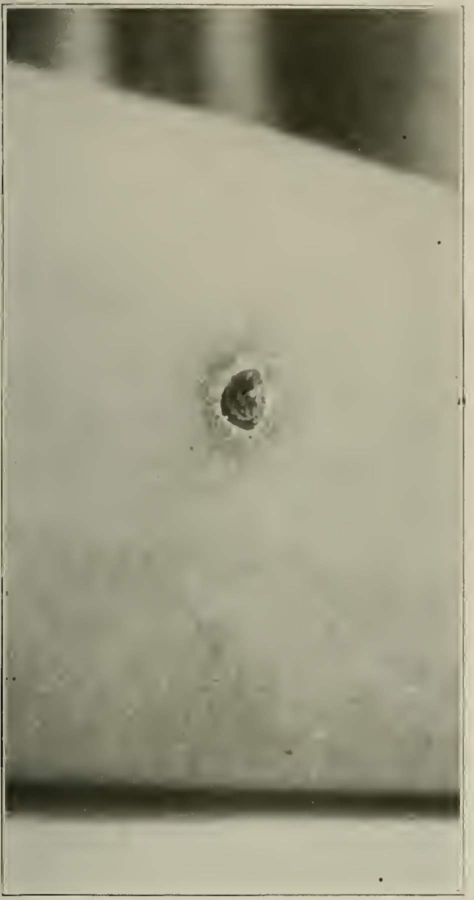

Fig. 9.—Eighteen days after application. Raising and separation of the yellowish brown crust. Beginning fading of the erythematous area leaving a pigmented border.

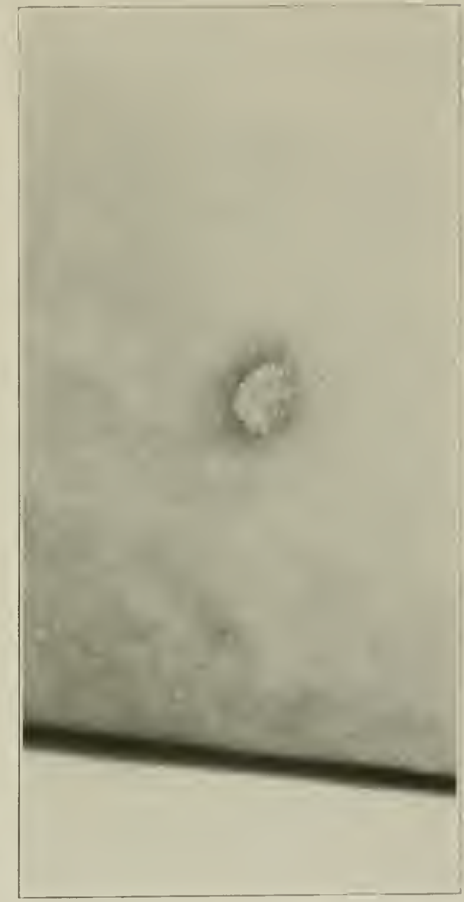

Fig. 10.—Nineteen days after application. Base of lesion after complete separation of the heavy crust of the eschar. Granulation tissue base.

Same day, 12:30 P.M. Twenty-two hours after application. (Fig. 4.) At this time the vesicle covered no greater area but was 4 mm. high and still very tense. Its fluid content had become slightly cloudy or opalescent. With a hand lens the base of vesicle can be seen through the fluid content and appears yellowish white, opaque and necrotic. Around the border of the inflamed base of the vesicle there is a definite secondary areola.

March 14, 1918, 12:30 P.M. Forty-six hours after application. (Fig. 5.) By this time there was nearly complete absorption of the fluid from the vesicle. The epidermal covering of the vesicle is thrown into fine wrinkles and folds and has taken on a yellowish brown tint. The zone immediately around the base of the vesicle is now pale pinkish white and about 1 mm. in width. Outside of this the flushed areola persists. The total width of the lesion is now but 17 mm.

March 15, 1918, 2:30 P.M. Seventy-two hours after application. (Fig. 6.) The central portion of the lesion measures 8x4 mm. and is of a bright yellowish brown color. Around this is a white zone 1 to 2 mm. in width. Outside of this is a zone of erythema most marked about the base of the collapsed vesicle and fading peripherally. The total width of the lesion is now 18 mm.

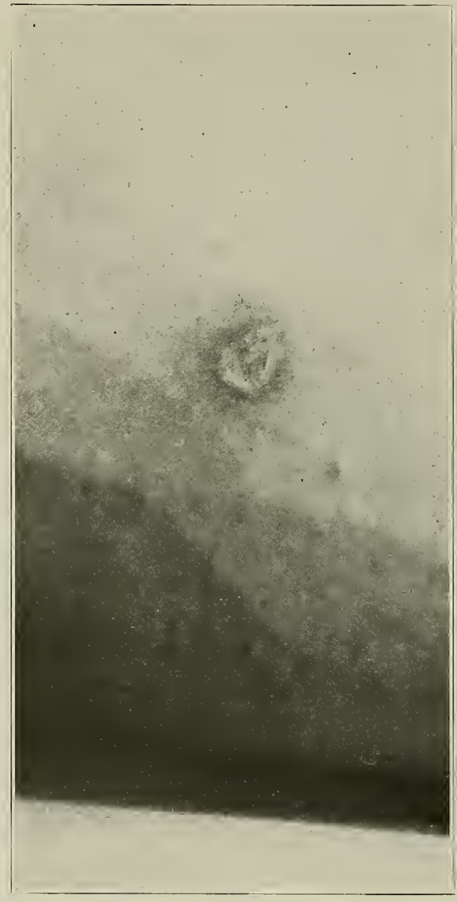

Fig. 11.—Forty-nine days after application. Scar with brown pigmented areola. Slight puckering of scar.

During the night of March 15 to March 16 the delicate wrinkled epidermis was rubbed off, leaving an excavated area with a grayish yellow-white moist base. The excavated area measured 6x4 mm. The border was somewhat irregular and slightly overhanging. The white zone, about 1 mm. in width, still persists at the border and the erythematous zone outside of this is about the same width as before. The base became slightly glossy upon drying. Fig. 7 was taken at 5:30 P.M., March 16, 1918.

March 17, 1918, 9:00 P.M. Total excavated area somewhat diminished. Border smoother. Floor not quite so deep. Total width of lesion is now 15 mm.

March 21, 1918, 4:00 P.M. A brownish crust representing the necrotic base is beginning to loosen at the edges where it is white and slightly desquamating. About this is a marked erythematous areola, 4 mm. wide. (Fig. 8.)

March 22, 1918, 9:00 A.M. During the night there was marked itching, the only pronounced subjective symptom so far noted. The crust loosened entirely and came off. Beneath the crust there was a small amount of thin purulent fluid. The erythematous zone is less marked. The base of the excavated area is again dry and covered with a yellowish brown crust. The margin of the excavation is whitish with edges slightly puckered. The central portion of the lesion measures 5x9 mm.

March 30, 1918. Since March 22, the area of excavation has gradually become covered with a yellowish brown crust which has now become elevated nearly 2 mm. above the surrounding surface. The zone of erythema is fading, leaving a yellowish brown pigmentation. The inner portion of this zone is shiny and somewhat puckered and there are a few minute desquamating scales at the border of the dense crust. The entire width of the lesion including the zone of pigmentation is 3 cm., the reddened, somewhat shiny zone, is 2 to 3 mm. in width, the scaly desquamation about 1 mm., and the elevated crust 4x7 mm. (Fig. 9.)

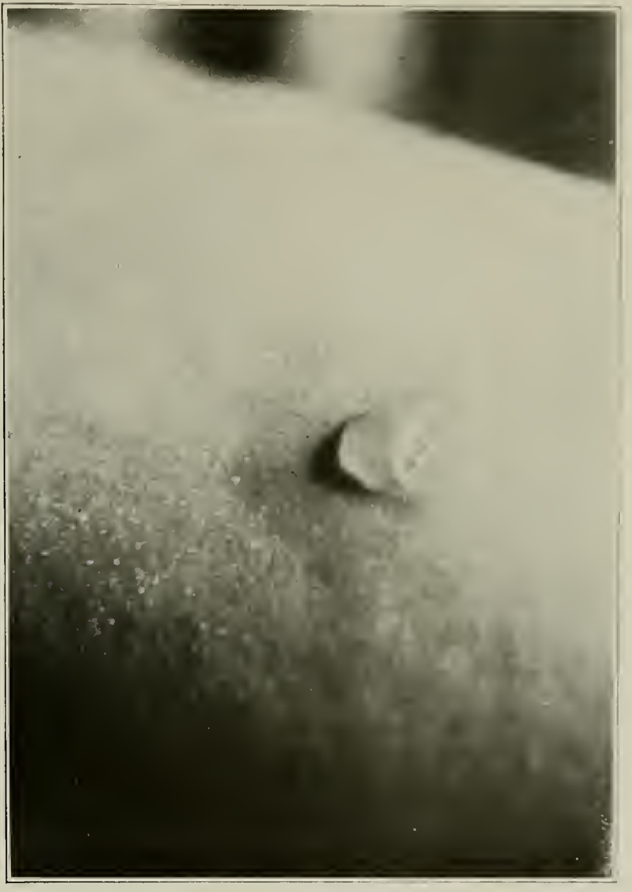

Fig. 12.—Typical "mustard gas" vesicle. About twenty-two hours after application. Photograph somewhat enlarged to show details of the vesicle.

April 1, 1918. The dark crust or scab became loose and came away leaving a white, dry, slightly granular area nearly flush with the surface of the skin. This measured 4x8 mm. (Fig. 10.)

May 1, 1918. Healing is now nearly complete, the lesion consisting of a thin scar, pinkish white in the central portion and whiter, more opaque, at the margin, with very slight puckering. Around this is a brown pigmented areola. The whole area, however, is redder than normal skin. (Fig. 11.)

Microscopic Appearances

The changes in human skin were studied microscopically from one-half hour up to four weeks, including the development of the vesicle and beginning eschar formation. As the lesions at one-half hour, eighteen hours, and thirty-six hours represent three distinct stages, these will be described in detail.

LESION ONE-HALF HOUR AFTER APPLICATION

EPIDERMIS.—The horny layer is relatively thicker than normal and split up into flat scales and layers, loosening readily from the stratum lucidum. The stratum lucidum has a slight brownish color. The granular layer is flattened; the cells drawn out parallel to the surface; the nuclei are pyknotic. The stratum germinativum is markedly shrunken, in many places only one-third to one-half as wide as normal, its nuclei pyknotic and the cytoplasm shrunken about the nuclei. Occasional vacuoles are found in the lowest layers, but the most marked change is the shrunken appearance of the whole epidermis, both cytoplasm and nuclei. At the border of the lesion the epidermis passes gradually into the normal condition.

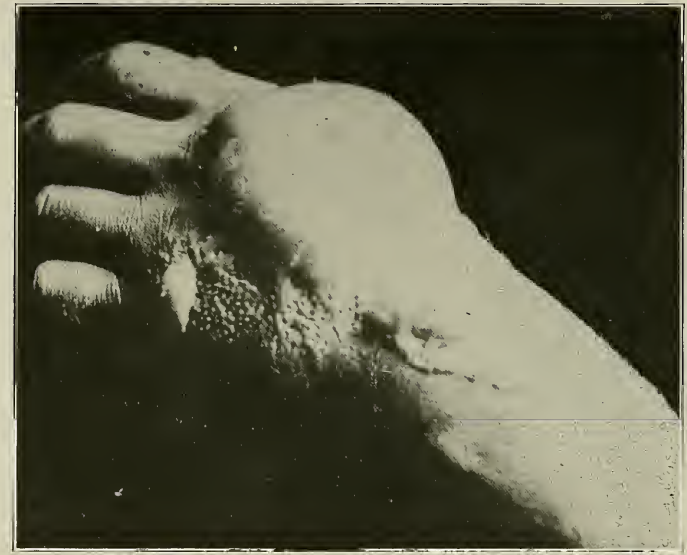

Fig. 13.—Hand, twenty-four hours after exposure to mustard gas vapor, while repairing and doing pipe-fitting on a small gas tumbler. Erythema developed five hours after exposure and small blebs appeared after twelve hours. By twenty-four hours the back of the hand showed a large bleb, as seen in the photograph.

PAPILLARY LAYER OF CORIUM.—In the central part of the lesion, the capillaries are contracted and contain but little blood. In scattered capillaries the red blood cells are agglutinated and stain with eosin as bright red hyaline masses. Such agglutination thrombi, however, are not a common feature of the picture and in the larger vessels thrombosis does not occur. The endothelium of the capillaries of the papillary layer shows marked pyknosis, karyorrhexis and disintegration of the nuclear chromatin. Chromatin dust is found around many of these capillaries and also many of the connective tissue cells of the upper portion of the papillary layer show marked karyorrhexis. The cytoplasm of many of the endothelial cells of the capillaries is vacuolated, showing hydropic degeneration or edema. About these capillaries there is a clear space due to a

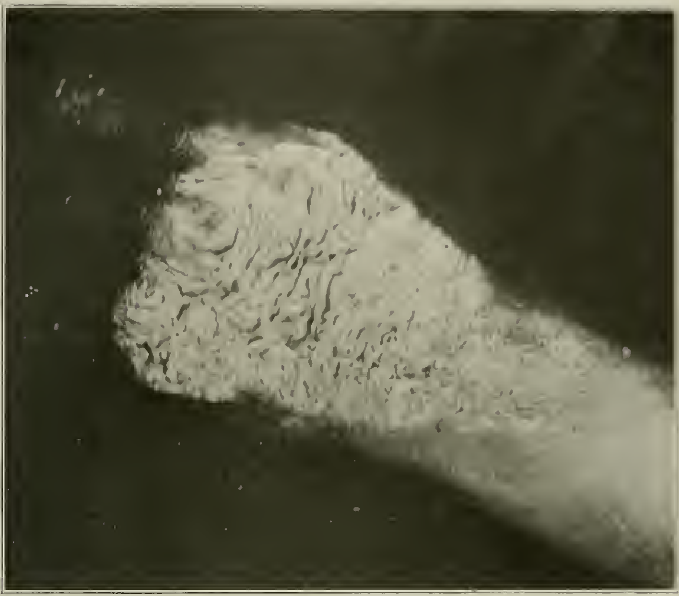

Fig. 14.—Same hand as in preceding figure, on sixth day after exposure to mustard gas.

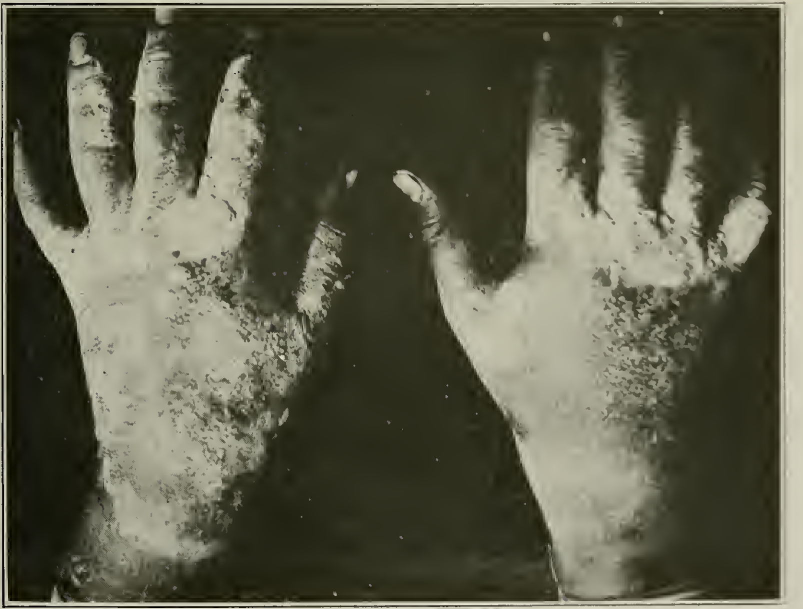

Fig. 15.—Mustard-gas burns of both hands, six days after exposure, in a chemical laboratory assistant.

perivascular edema. Around some capillaries this is very marked. Many of the capillaries show diapedesis of leucocytes along their course (Fig. 17), but in the central part of the lesion there is practically no hemorrhage and the vessels are conspicuous for their contraction and anemia.

Corium Proper.—The vessels running through the corium show similar changes in their endothelium but there is little leucocytosis or white cell migration. The larger vessels contain more blood. No thromboses or hemorrhages are present. The lymphatics are dilated and the nerve trunks show karyorrhectic nuclei and edema.

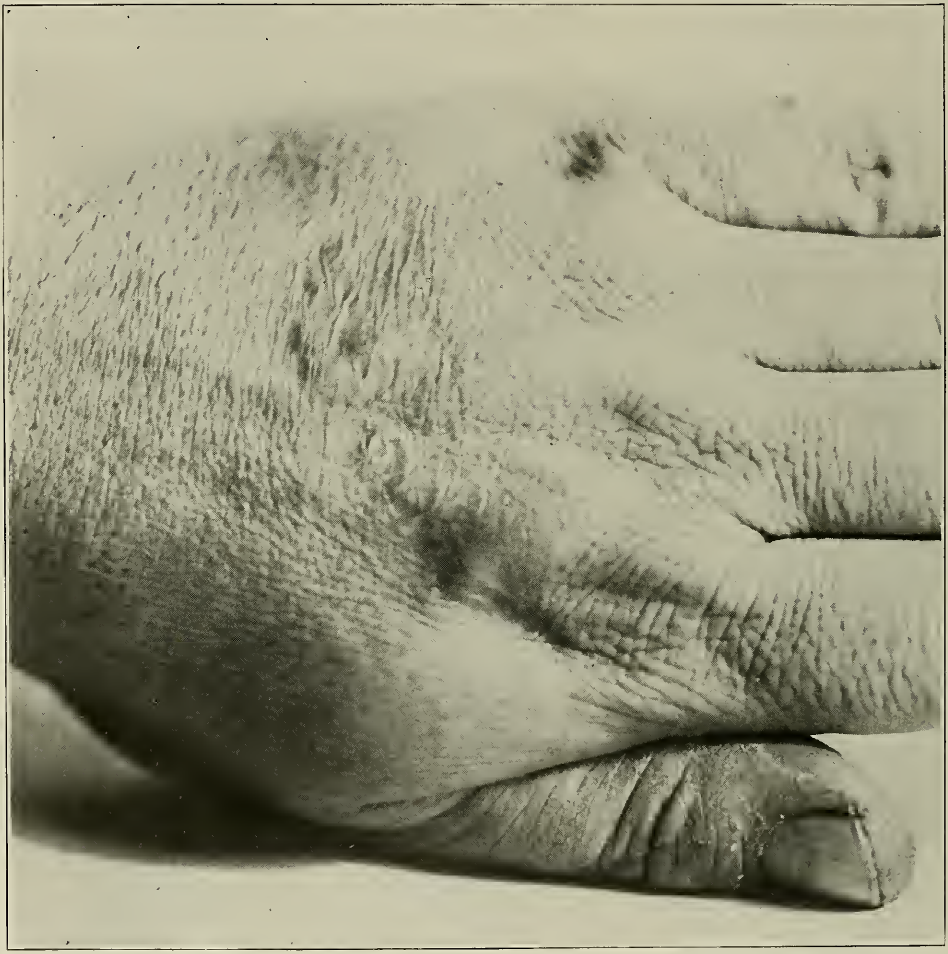

Fig. 16.—Scar on back of hand six months after accidental burn with a dilute solution of dichlorethylsulphide dropped upon back of hand and immediately washed away. Chemist. Burn exhibited stages of vesicle and eschar formation similar to those described in the above protocol, followed by very slow healing.

Hair Follicles.—Along the hair follicles the squamous epithelium shows changes similar to those of the surface and the capillaries about the hair follicles also show changes similar to those described above. In the neighborhood of the hair follicles the corium is affected more deeply than elsewhere, showing a distinct penetration through the hair follicles.

Sweat Glands.—The epithelium of the sweat glands shows no apparent changes, although the vessels about them show changes similar to those described above.

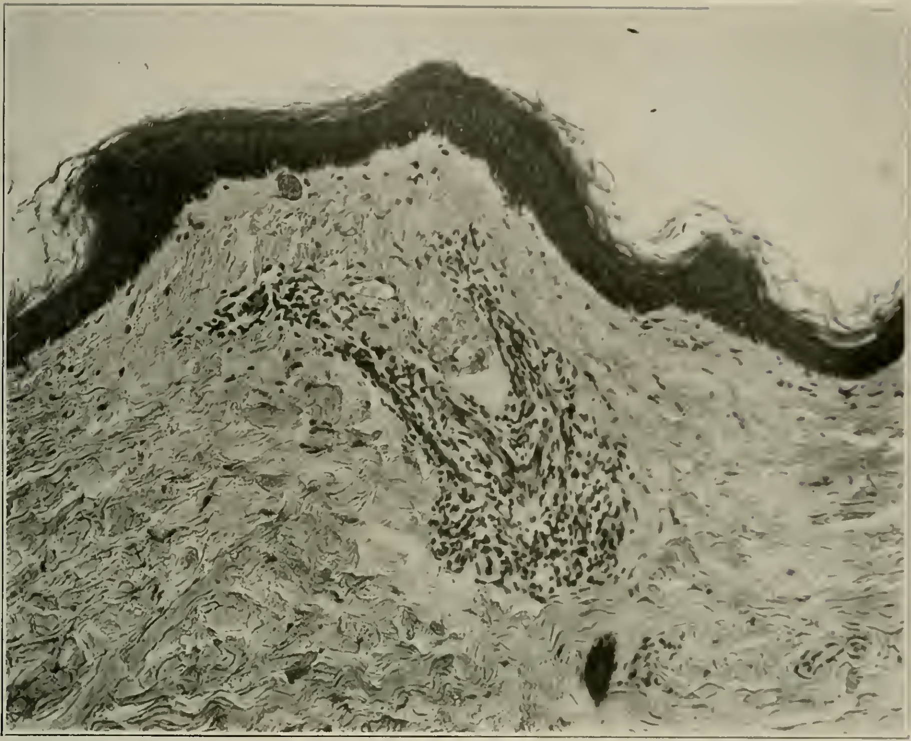

Fig. 17.—Human skin one-half hour after application of mustard gas. Shrinking and pyknosis of epidermis with desquamation of horny layer. Capillary changes as described in the text, including well-marked migration of leucocytes.

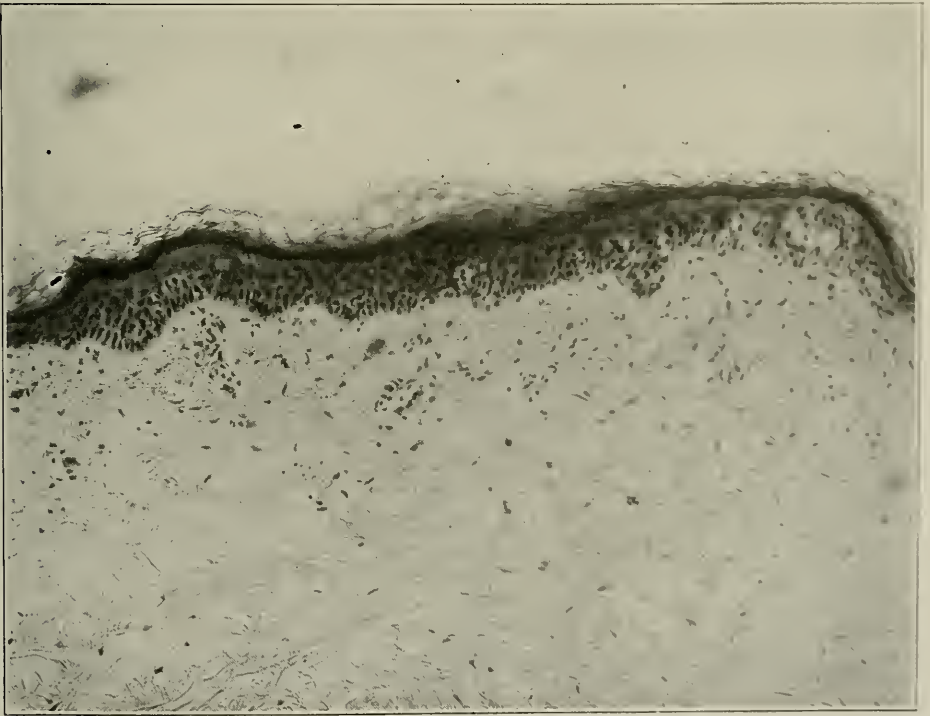

Fig. 18.—Human skin eighteen hours after application. Transition between slightly damaged epithelium and epithelium showing hydropic degeneration. Early blister formation.

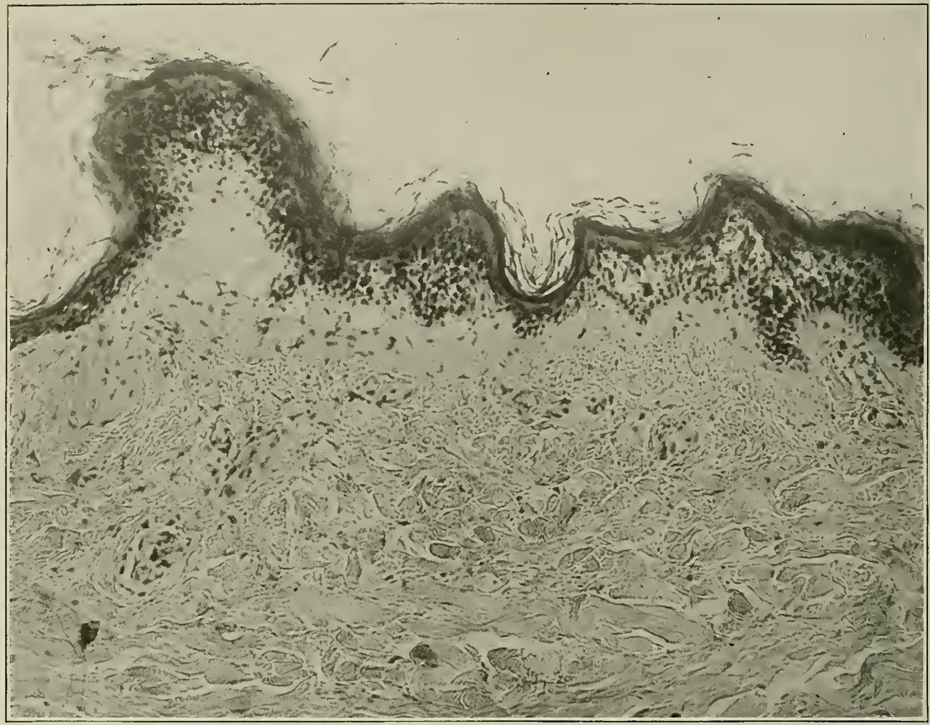

Fig. 19.—Human skin eighteen hours after application. Early vesicle formation.

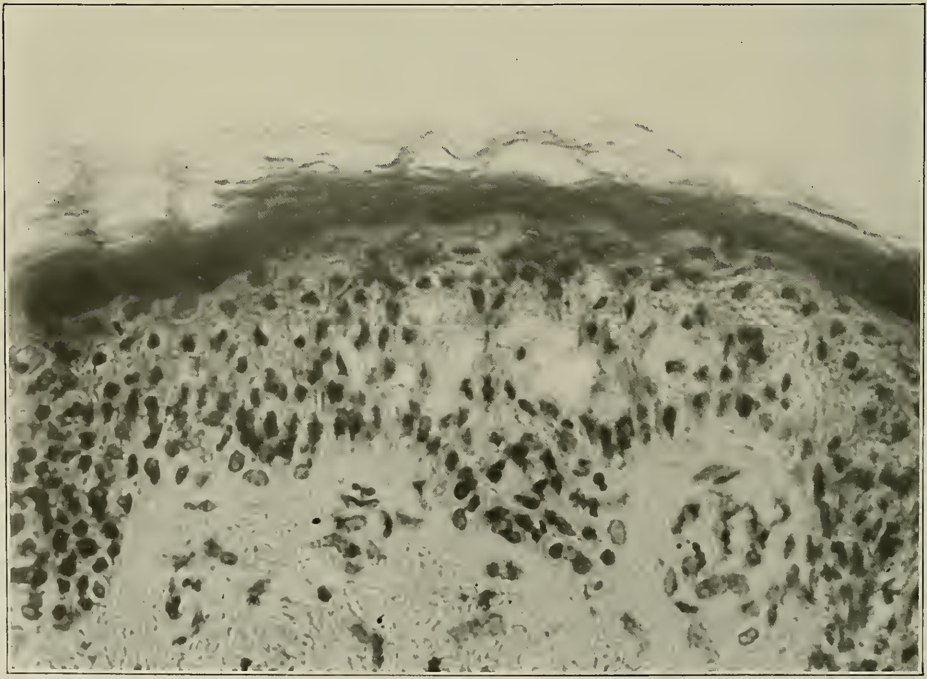

Fig. 20.—Human skin eighteen hours after application. High power view of hydropic change with early vesicle formation.

Sebaceous Glands.—Shrinking and pyknosis of cells similar to that seen on the surface.

In the transition border there are small hemorrhages by diapedesis.

Lesion Eighteen Hours after Application (Figs. 18, 19, 20, 21)

Epidermis.—In the central part of the lesion there is a marked liquefaction and hydropic change in the cytoplasm of the epithelium. This varies greatly in degree. The horny layer is in part desquamated and loosened, the stratum lucidum is widened and more dense than normal and stains brownish red. Over many of the papillæ small vesicles have already formed, the majority of the epithelial cells having undergone liquefaction. In some places the epidermis is lifted from the papillæ by the collection of fluid beneath it. The liquefaction of the cell cytoplasm extends deep down into the hair follicles and into the sebaceous glands. The stratum germinativum has lost its continuity in many places and the cells are completely necrotic.

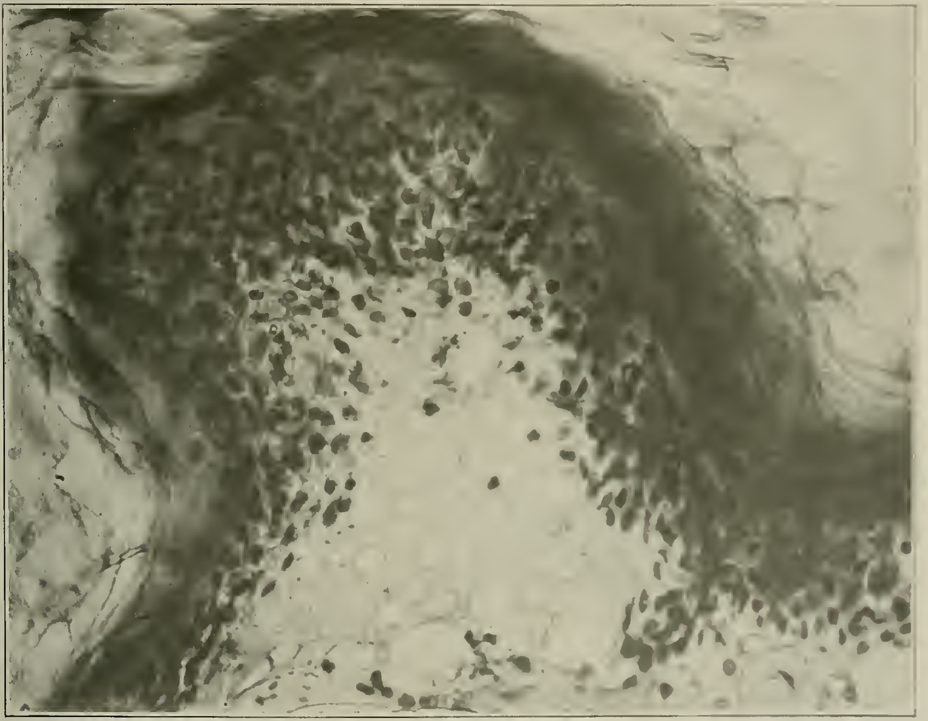

Fig. 21.—Human skin eighteen hours after application. High power view of small vesicle. Separation of epidermis from papillary layer.

Papillary Layer of the Corium.—The connective tissue is edematous, stains bluish, and contains many degenerating nuclei. There is an increase in the number of wandering cells and many of these show karyorrhexis. Around all the capillaries there is a zone of edema and small-celled infiltration. Small hemorrhages by diapedesis are scattered through the papillary layer and upper portion of corium, particularly around the hair follicles.

Corium Proper.—The blood vessels contain more blood than in the earlier

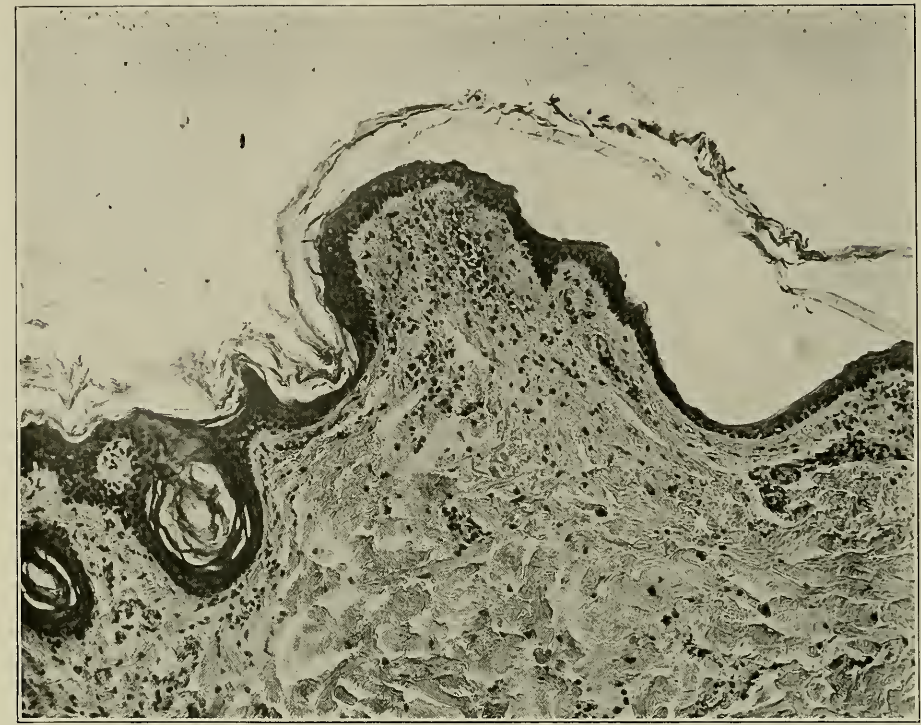

Fig. 22.—Human skin thirty-six hours after application. Vesicle formation in epidermis and leucocyte infiltration of papillæ.

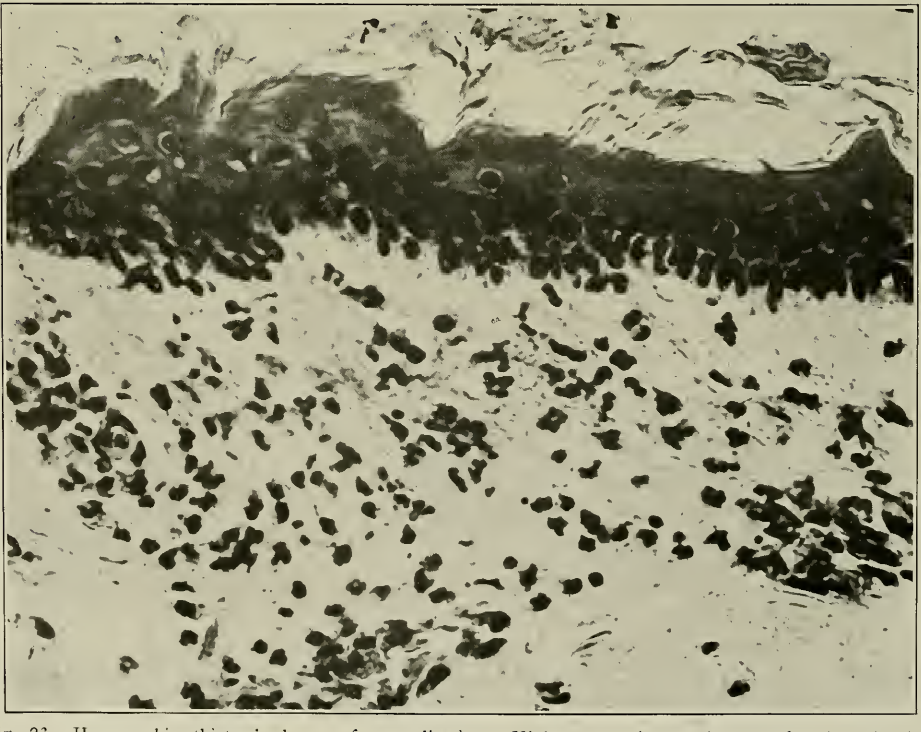

Fig. 23.—Human skin thirty-six hours after application. High power view at border of lesion showing changes in epidermis and leucocyte infiltration and edema of papillary layer.

lesion, particularly the deeper ones. The larger ones show a marked congestion and the lymphatics are dilated with a lymph rich in albumin. Around the hair follicles the edema, liquefactive changes, and hemorrhages are more marked than elsewhere. The sweat glands show a marked edema of the interstitial connective tissue, congestion of the capillaries, leucocyte infiltration and small hemorrhages by diapedesis. Some of the glands show a marked necrosis of the epithelium but these changes vary greatly in degree.

SUBCUTANEOUS TISSUES.—The vessels are congested, lymphatics dilated and there is edema of the adipose tissue. The vascular changes extend along the smaller capillaries even into the subcutaneous tissue.

LESION THIRTY-SIX HOURS AFTER APPLICATION (FIGS. 22, 23)

EPIDERMIS.—Horny layer more compact but ragged, in many places infiltrated with leucocytes. Epidermis nearly completely necrosed, in some places lifted from the papillary layer. The remaining nuclei are markedly pyknotic or fragmented. In many areas only the lowest layer of nuclei persists. There are also collections of fluid between the horny layer and the portions of rete remaining.

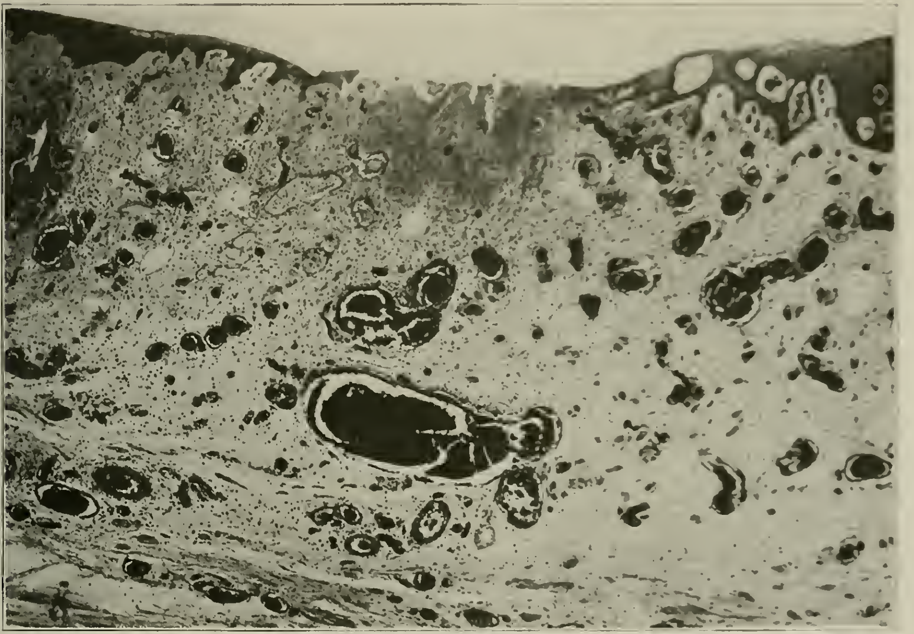

Fig. 24.—Droplet lesion of mustard gas on human skin. Seven days after application. Low power view showing area of necrosis of epidermis and upper portion of the corium with intense hyperemia of the surrounding vessels. Moderate edema and very little small-celled infiltration.

PAPILLARY LAYER.—The papillary layer shows marked edema, the capillaries are congested and there are many hemorrhages by diapedesis. The entire papillary layer is infiltrated with leucocytes, many of which show karyorrhexis.

CORIUM.—There is a leucocyte infiltration throughout the entire corium but less marked than in the papillary layer. It is most marked around the hair follicles and around the sebaceous glands and sweat glands. The congestion and edema are also most marked around these structures. Some of the smaller vessels show marked necrosis of the wall with leucocyte infiltration and diapedesis. Scattered areas of edema and small celled infiltration extend even into the subcutaneous tissue where the vessels are markedly congested.

Later Stages in Human Skin

Inasmuch as the later stages in human skin parallel those in the lower animals and as the specific differences between the action of mustard gas on human skin and on the skin of the rabbit, guinea pig and cat exist only in the early stages, it seems necessary here to omit a more detailed description of these changes and to summarize them as follows:

1. About forty to fifty hours after application collapse of vesicles and progressive necrosis.
2. About seventy-two hours after application progressive necrosis and beginning eschar formation.
3. Four to six days after application, necrosis complete, beginning separation of slough. Edema and hyperemia persistent. Fig. 24 shows the microscopic appearances of a droplet lesion on human skin at one week after application. In the center the epidermis is completely necrosed and desquamated; the necrosis extends some distance into the corium; the surrounding area is intensely hyperemic; there is moderate edema, very little leucocyte infiltration, and no evidences of repair.
4. By the nineteenth day, complete separation of slough. Slow healing and scar formation.
5. For an indefinite period, congestion and pigmentation.

All of these descriptions apply to the effect of a standard drop of pure mustard gas in the absence of infection. The course will naturally vary with the concentration, amount, time, etc. In very mild mustard gas lesions, appearing only as hyperemias, with intact epidermis, the microscopic examination may show a complete necrosis of the papillary layer of the corium with the exception of the chromatophores which become larger, increased in number and heavily pigmented. The pigmentation is due to melanin and not to blood pigment. This necrosis of the upper part of the corium explains the secondary production of vesicles through slight trauma.

Animal Experiments

The rabbit, guinea pig, and cat were employed for these experiments. The skin of the belly was shaved and standard drops were applied after the irritation from shaving had subsided. The character of the tissue lesion and the reaction in these animals, proved, in the early stages, to be essentially different from the lesions in human skin. For the purpose of brevity and conciseness the protocols are condensed as below.

Rabbit.—Within two hours after application of the standard drop there develops a very marked edema, much larger than the area touched by the drop of mustard gas. This edema is subcutaneous, appearing as a definite tumor mass, rather sharply circumscribed, over which the cuticle can be moved. The surface of the area appears gray and cloudy, the skin losing its normal translucency and appearing as if cooked. In some cases the blanching appears to extend into the deeper portion of the skin. About this gray area there is but slight hyperemia. By the third day after the application, the epidermis over the area undergoes complete necrosis and there is formed a slough without any vesicle formation. Vesicles were never observed in the rabbit. This slough is held on apparently by the hairs. It gradually is elevated, separates, and contracts, and may not be cast off for three or four weeks. When shed, the lesion below is practically healed. The most striking thing is the marked edema at the beginning, the persistence of this edema without vesicle formation, and the slow healing in the absence of infection.

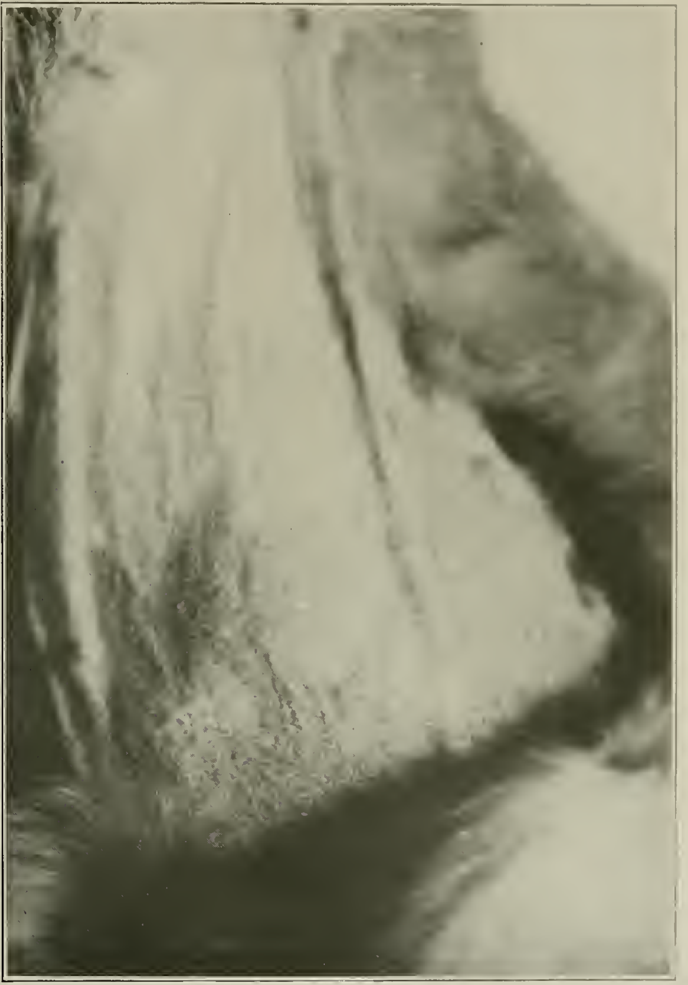

Fig. 25.—Rabbit. Application of mustard gas at 11:30 A.M. Droplet used was slightly larger than the standard. Marked subcutaneous edema as seen at 4:00 P.M. on the same day.

Various protective experiments were tried out, a number of substances being used to prevent the lesion or lessen its severity—washing with water, soap and water, lead acetate, lead acetate and silver nitrate, zinc oxide ointment, zinc oxide paste, bleaching powder, sodium sulphide, tincture of green soap, potassium permanganate. The application of most of these substances five minutes after the application of the mustard gas lessens the edema and renders the lesion more diffuse but does not prevent necrosis. The use of potassium permanganate resulted in even greater edema than the untreated control while strong sodium sulphide solution was found to be disadvantageous because of the necrosis produced. (Figs. 25, 26, 27.)

Guinea Pig.—Practically identical results were obtained in the guinea pig with the standard drop of pure mustard gas; namely, within a few hours marked subcutaneous edema followed in a few hours by necrosis of epidermis and papillary layer without vesicle formation and exhibiting very slow healing.

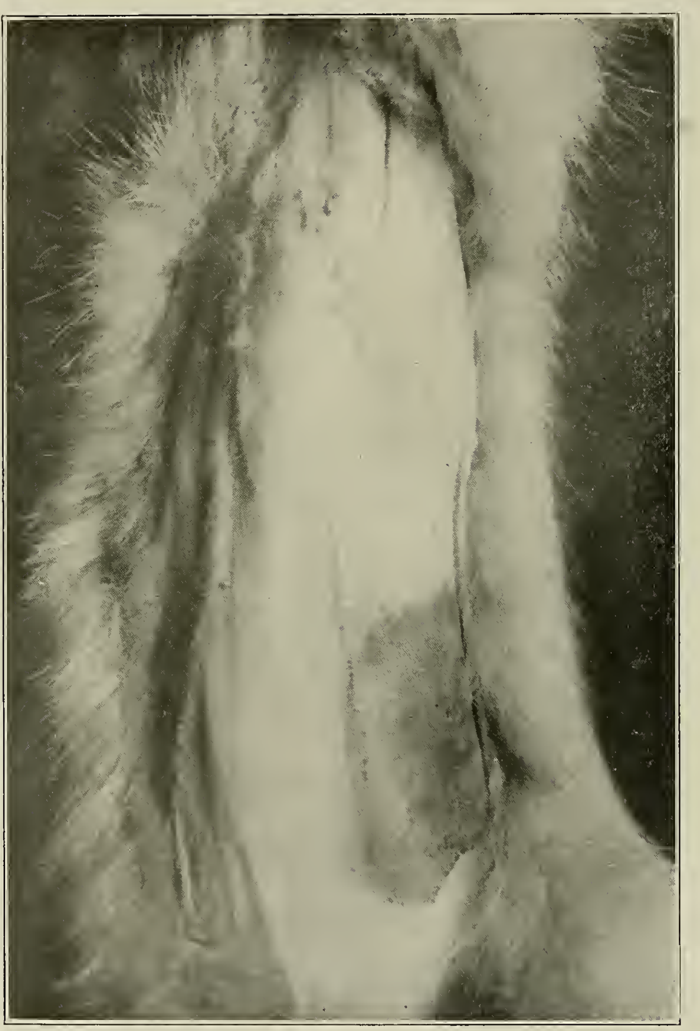

Fig. 26.—Rabbit. Skin of belly shows results of four applications of standard drops of mustard gas. Above two areas, of typical edema, the one on the rabbit's right untreated, the one on the left washed off in five minutes by water. The latter is more diffuse, larger in area, but less intense. Below on the rabbit's right, an area washed after five minutes with soap containing an excess of free alkali. This area shows the least reaction. On the lower left is an area treated after five minutes with potassium permanganate. The reaction here is the most marked.

Cat.—The same results were obtained as for rabbits and guinea pigs. Subcutaneous edema without vesicle formation, followed by necrosis and slow healing.

Microscopic Pathology of Animal Lesions

The changes observed in the development of the lesions in the rabbit, guinea pig, and cat are essentially the same and are summarized here as follows:

1. Stage of Marked Edema.—The most striking feature of this stage is the intense edema which although sharply localized to the subcutaneous tissue and fascia, extends also into the muscle of the abdominal wall. The connective tissue fibrillæ are widely separated and the tissue spaces are filled with a heavy albuminous precipitate staining deep pink with eosin. The muscle fibers of the abdominal wall are separated, and even in two hours there is a leucocytic infiltration into the muscle. The edema extends 0.5 to 1 cm. below the epidermis. The epidermis is shrunken, cells pyknotic and in the central portion of the lesion completely necrotic. In the upper layer of the corium numerous degenerating nuclei are seen. The blood vessels show degeneration of the endothelium with small hemorrhages by diapedesis and leucocyte migration. Around each vessel there is an area of edema. There is, however, no vesicle formation in or beneath the epidermis as in the human cases. The changes are more uniformly diffuse in

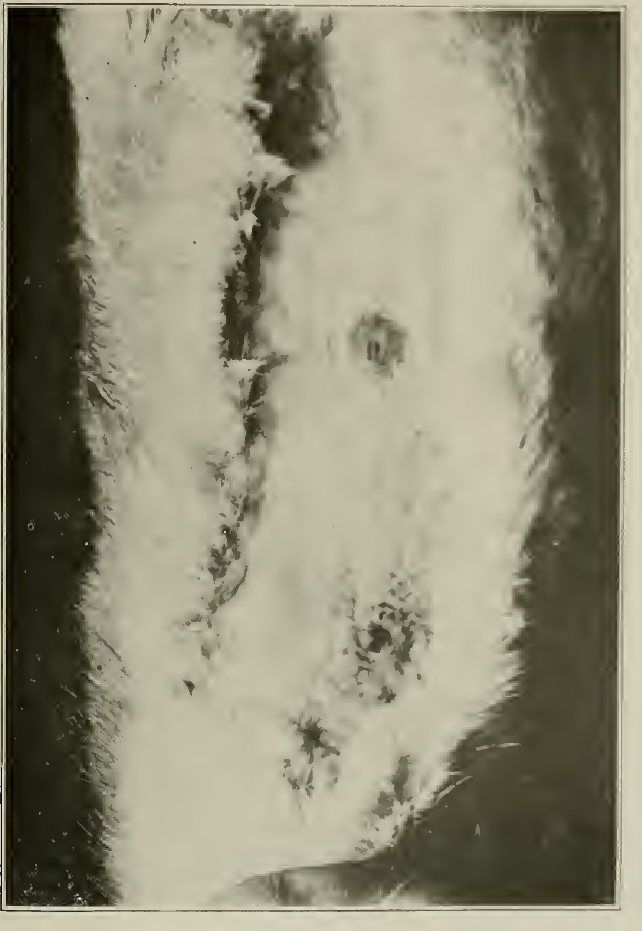

Fig. 27.—Rabbit. Two areas of mustard-gas application. Advanced eschar formation.

the animal than in the human skin and the depth of penetration greater. The localized penetration along the hair follicles, so prominent in the human skin, does not show in the animal skin, the greater number of hair follicles permitting a more uniform access of the liquid. There are no thromboses in the damaged area. The hemorrhages are relatively small and, as in the human skin, the vessels in the immediate lesion are contracted and anemic. Around the borders of the lesion they show marked congestion.

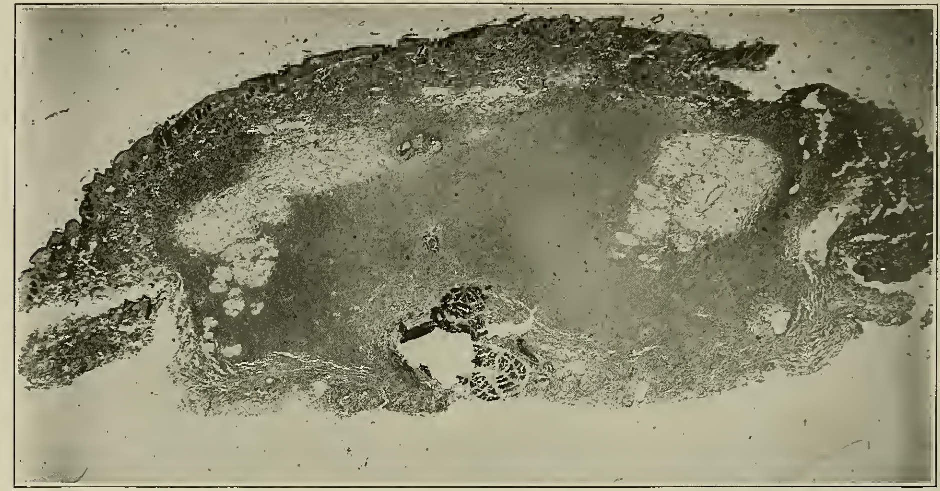

Fig. 28.—Rabbit. Low power view of mustard-gas lesion in rabbit two hours after application. Extreme subcutaneous edema. Epidermis but slightly changed.

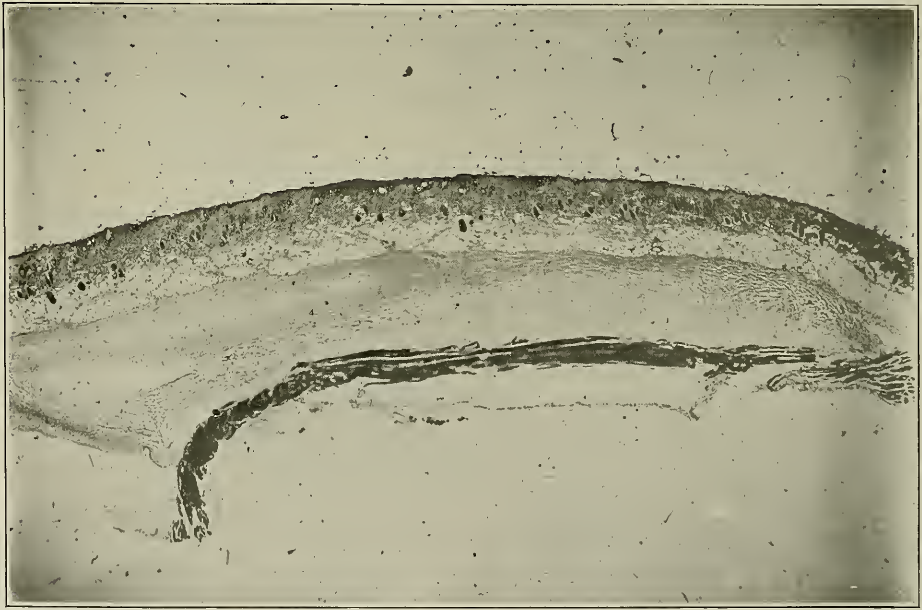

Fig. 29.—Guinea pig. Low power view of mustard-gas lesion five and one-half hours after application. Extreme subcutaneous edema. Epidermis necrosed in center of lesion.

2. Stage of Necrosis.—The necrosis of the epidermis and of the underlying

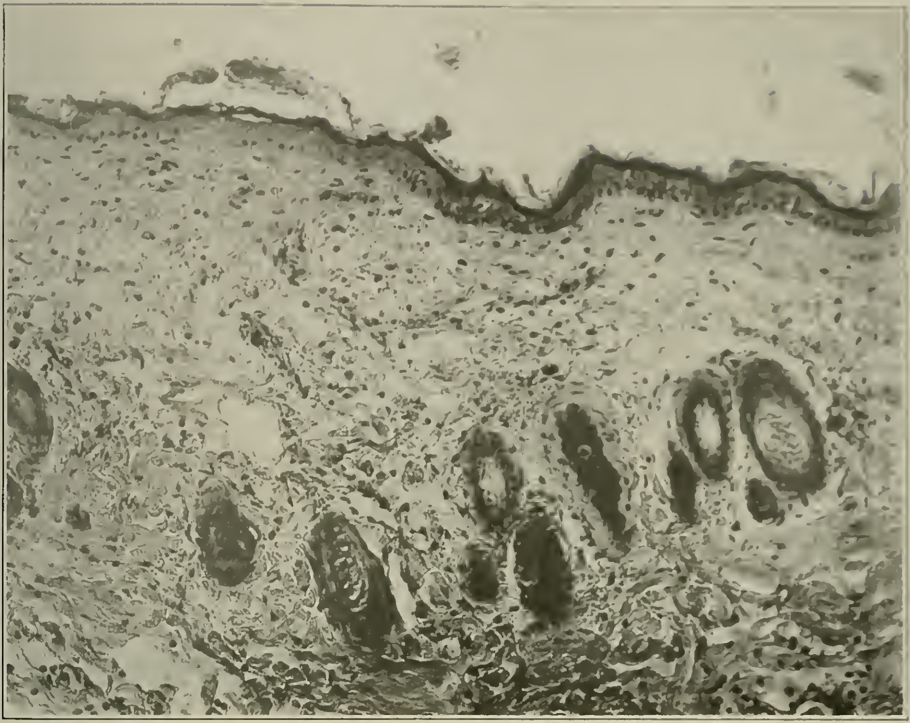

Fig. 30.—Rabbit. Border of lesion two hours after application. To the right of the middle the epidermis is still living, to the left nearly completely necrosed, necrosis extending into the upper portion of the corium. Early edema.

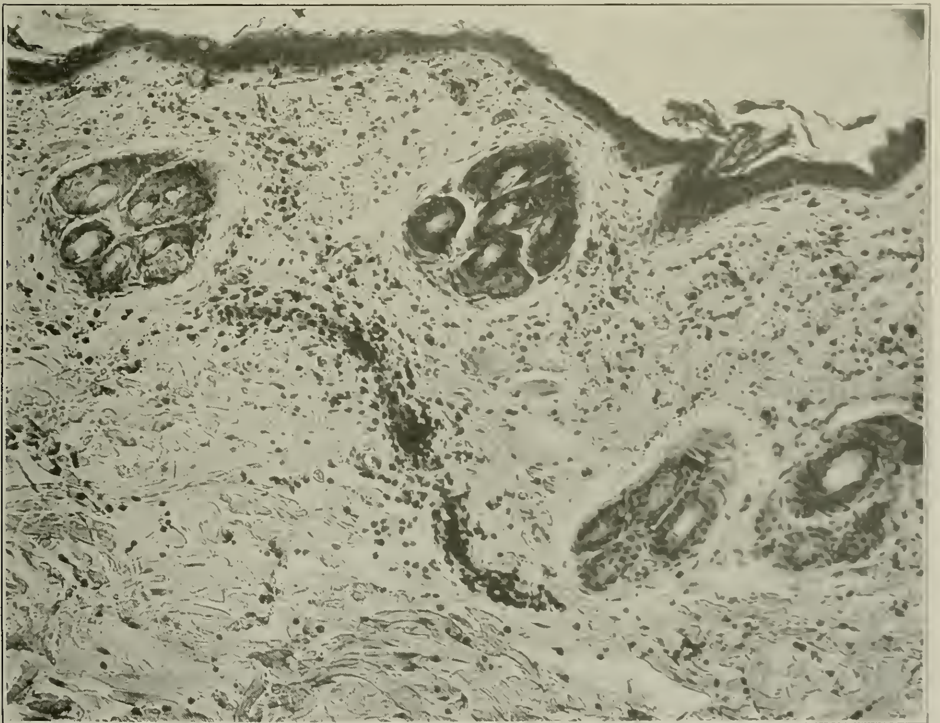

Fig. 31.—Rabbit. Two hours after application. Changes in epidermis and corium. Marked vascular change with beginning migration of leucocytes. Small hemorrhages by diapedesis. Early edema.

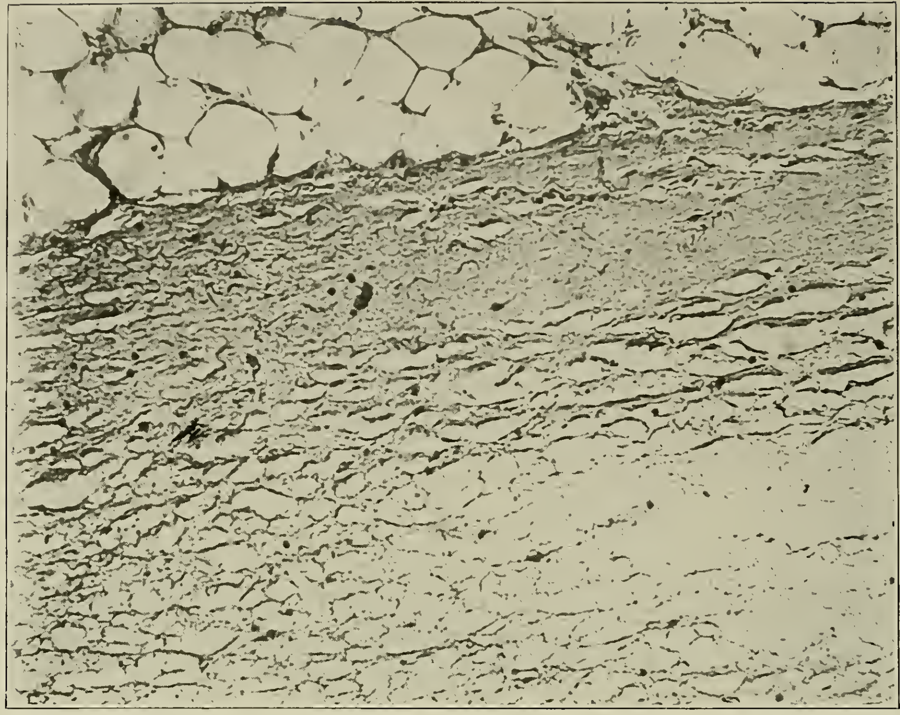

Fig. 32.—Guinea pig five and one-half hours after application of mustard gas to skin of abdomen. Deep subcutaneous edema.

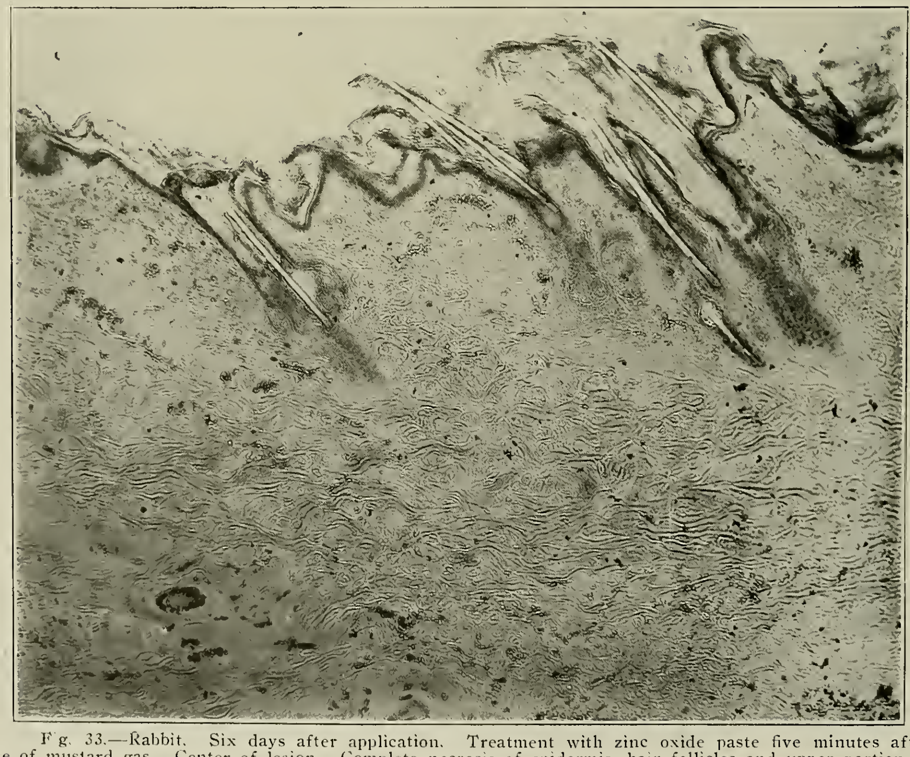

Fig. 33.—Rabbit. Six days after application. Treatment with zinc oxide paste five minutes after use of mustard gas. Center of lesion. Complete necrosis of epidermis, hair follicles and upper portion of corium, extending even to the sweat glands. No reaction.

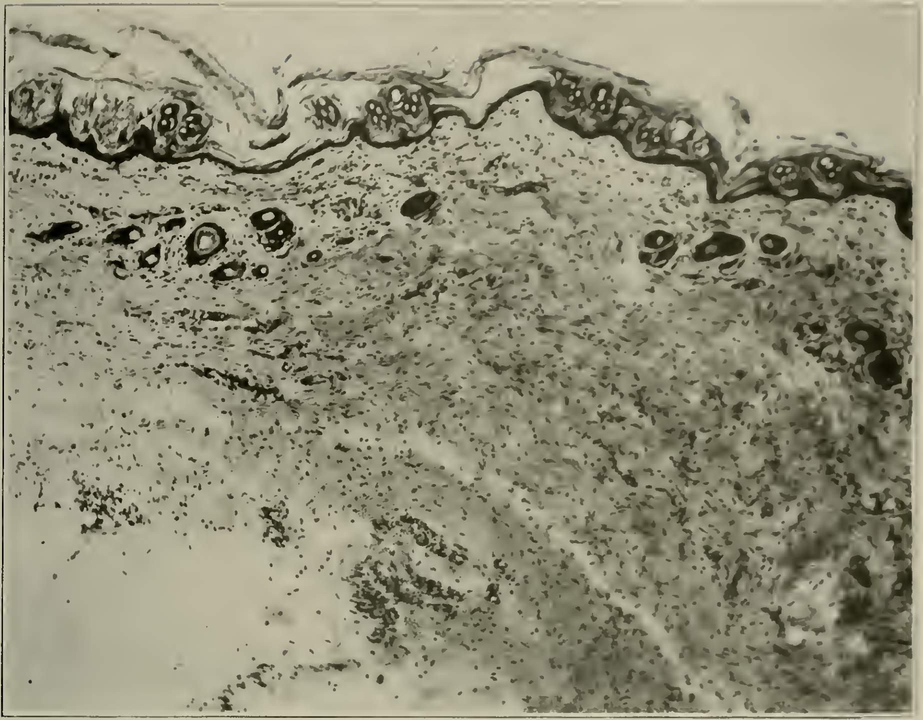

Fig. 34.—Rabbit. Six days after application. Treatment with zinc oxide ointment five minutes after application of mustard gas. There was no edema stage. Epidermis is dead and there is a moderate inflammatory reaction in the corium. Reaction much less intense than in control.

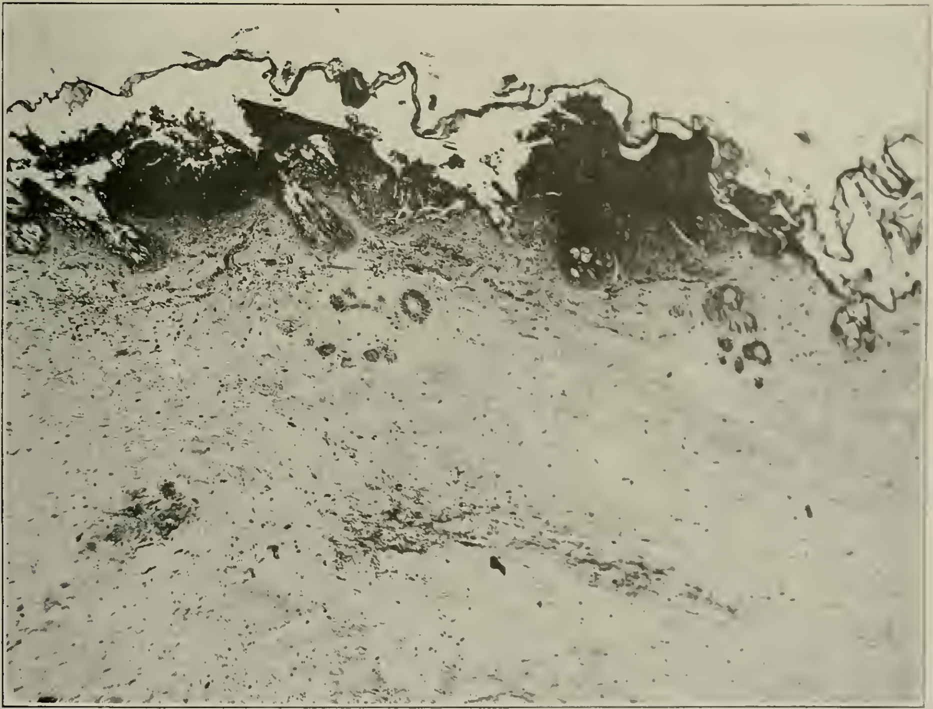

Fig. 35.—Rabbit. Six days after application. Treatment after five minutes with two per cent solution of silver nitrate and five per cent lead acetate. Primary edema was nearly completely controlled but necrosis six days after is marked, extending deep into the corium, with more rapid separation of the slough.

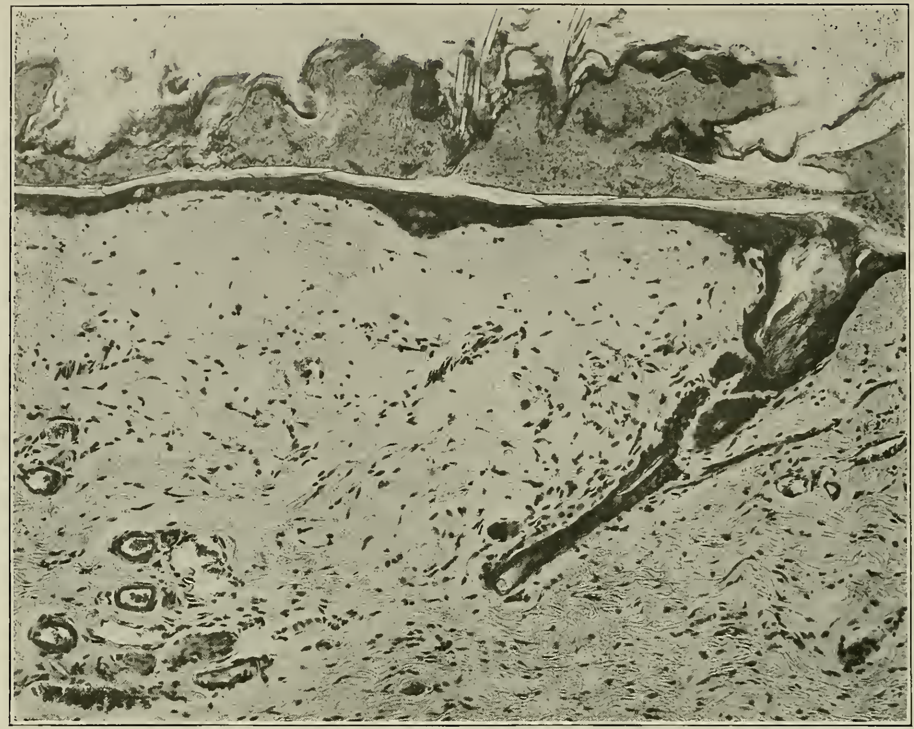

Fig. 36.—Rabbit. Periphery of same lesion as Fig. 35. Area of less damage.

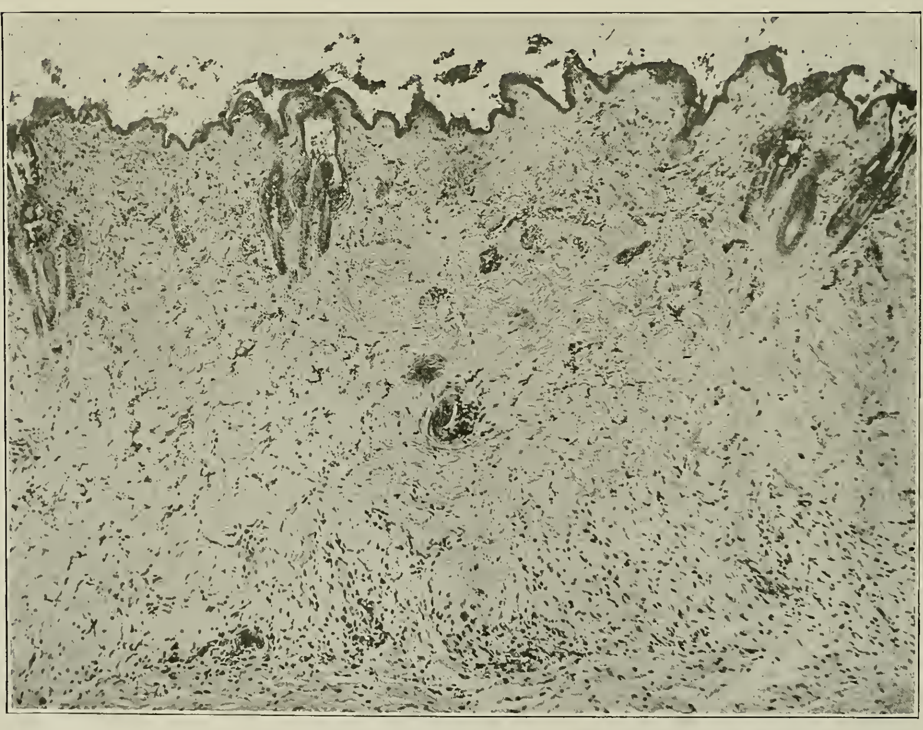

Fig. 37.—Rabbit. Six days after application, untreated. Border of lesion. Necrosis less marked. Beginning repair.

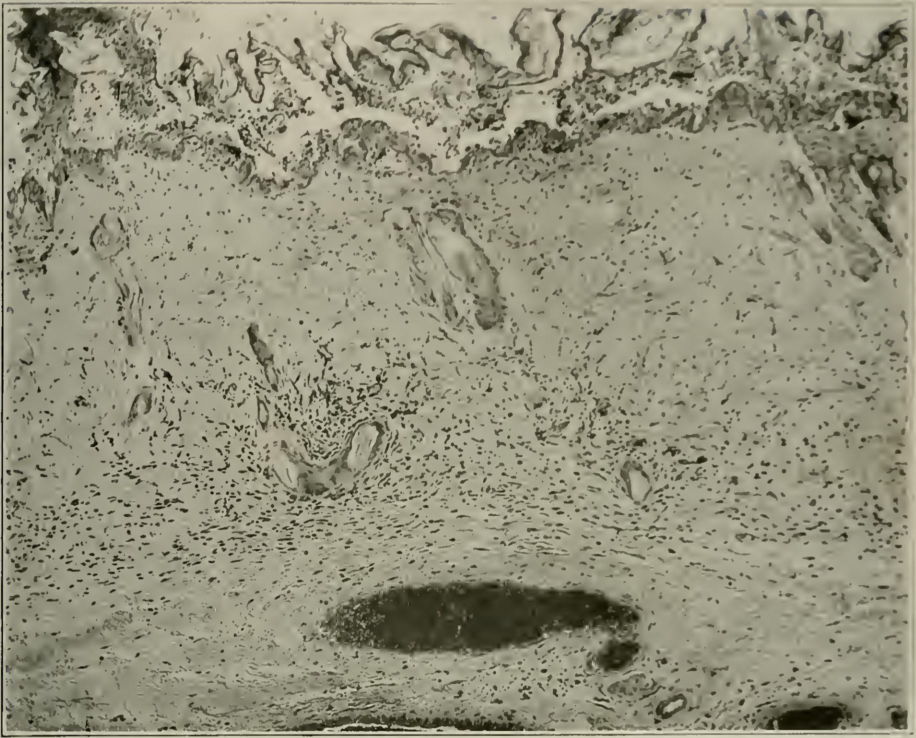

Fig. 38.—Rabbit. Six days after application, untreated. Intermediate zone. Separation of necrotic epidermis and papillary layer with infiltration of leucocytes into the necrotic tissue. Fibroblastic proliferation in lower part of dermis with regeneration of hair follicles. Intense congestion of subcutaneous vessels

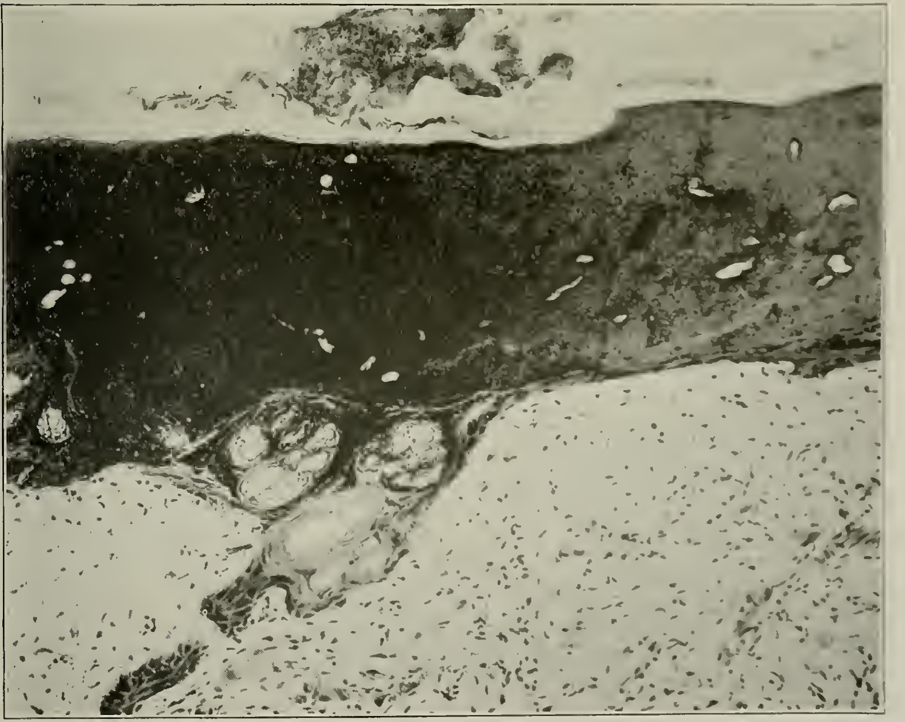

Fig. 39.—Rabbit. Six days after application, untreated. Adherent slough, representing the necrotic epidermis and upper portion of corium, involving the hair follicles.

tissues steadily becomes more prominent because of the loss of nuclei in the epidermis and upper part of the corium of the central part of the lesion. By the fifth and sixth day after the application of the mustard gas the edema has subsided to a marked degree and the central part of the lesion may be entirely without nuclei as far as the lower portion of the corium. It is bloodless, rather dry, and there is but little leucocyte infiltration. Surrounding this is a narrow zone of less marked necrosis and degeneration. This gradually becomes hyperemic and small hemorrhages by diapedesis may take place from the damaged vessels. In this area there is a more marked infiltration of leucocytes but this rarely becomes diffuse, the leucocytes remaining collected in the neighborhood of the vessels. Outside of this zone the tissues are hyperemic, somewhat edematous and show an increased number of wandering cells for some distance.

3. Stage of Eschar Formation.—There gradually begins a separation of the completely necrotic tissue from the living. This eschar consists of the dead epidermis and upper part of the corium, sometimes as far down as the lower borders of the hair follicles. This drys, contracts, becomes leathery, but is held in position by the hairs. There now develops in the neighboring living tissue a productive inflammation. The shrinking of the necrosed tissue and the demarcation, with the surrounding reparative inflammation, progress very slowly until there is a regeneration of the epithelium beneath the eschar. The latter remains adherent, usually until complete repair has taken place. The repair of the epidermis takes place chiefly from the cells remaining in the hair follicles.

(For the histologic changes in animal tissues see Figs. 28 to 39 inclusive.)

Cutaneous Lesions in Clinical Cases

A large number of mustard gas lesions of the skin were observed in men engaged in the manufacture and handling of dichlorethylsulphide. Some of these cases were extremely severe, two of them terminating fatally. All possible degrees of cutaneous lesions were seen. From these we choose the following seven cases for illustration:

Case I.—Private Mc. Seen one week after an exposure for forty minutes, in four shifts, to a strong concentration of mustard gas. Patient wore gas mask, rubber gloves, and rubber boots. One hour after exposure, after eating supper, he felt slightly nauseated, went out doors and began to feel very warm. Rolling up his sleeves he found his skin to be very red and, on opening his shirt, his chest was also seen to be very red. He immediately started for the emergency room, but on the way became much sicker and nauseated. He then took a kerosene rub and a hot water shower with soap, but as soon as the water struck him he vomited his supper. Then he took another shower, after which he vomited almost continuously for about five hours, altogether "about one-hundred times." At the same time his eyes began to smart intensely and for three days he was in intense agony from the eye pain. He developed a very dry throat, a hacking cough and difficulty in speaking. His severe symptoms lasted for three days but his voice remained husky and he had a bronchial cough for some time. The erythema of the skin persisted, but vesication and necrosis of the epidermis did not show for two days. When seen a week later, he presented the appearances seen in Fig. 152. Over the entire area of erythema, there was a branny desquamation of the epidermis and the skin appeared markedly pigmented, the pigmentation being deepest over the neck and forehead, region of the nipples, wrists, lower portion of abdomen, pubic region, and legs. In the hairiest part of the axillæ the lesions showed eschar formation. Eschars were also present at the bends of the elbows, around the genitals and in the popliteal spaces. The whole back desquamated. Over the back there were numerous small pustules. In the small of the back, just below the belt line, there were areas of necrosis covered with a greenish-gray crust. There were also minute pustules over the forearms

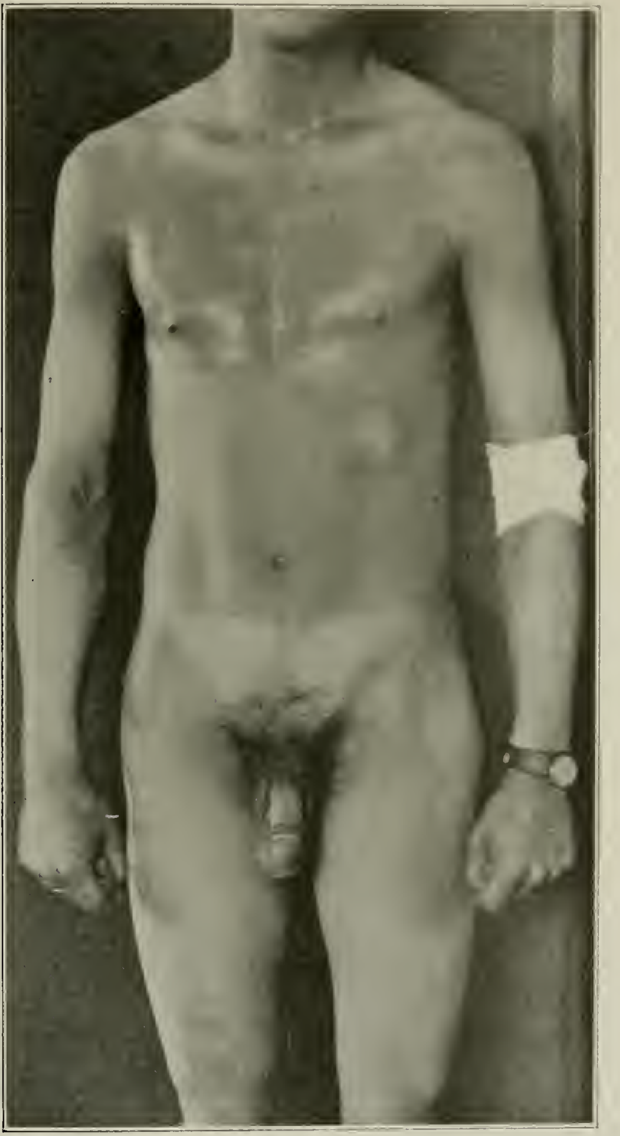

Fig. 40.—Diffuse erythema of the skin due to ten to twelve minutes exposure to strong concentration of mustard gas. Treated one week by the grease method with increasing infection of the dead skin, particularly around the genitals and anus. Change of treatment to the wet Dakin and saline methods resulted in prompt healing.

and legs, varying in size from a pinhead to a pea. There was an odor of putrefaction about the genitals. The surface of the entire glans penis was necrotic; the skin of the penis was edematous, desquamating, and showed numerous necrotic hair follicles. The skin of the scrotum was edematous, desquamating, with a necrotic, gangrenous surface, and exuding pus from all of the follicles. The inguinal lymph nodes on both sides were enlarged. The surfaces of contact between the genitals and the inner surface of the left thigh showed a deeper necrosis than elsewhere. Over the legs there was a large flaky exfoliation of the epidermis. The umbilicus was necrotic and infected. The ocular lesions are described in Chapter III.

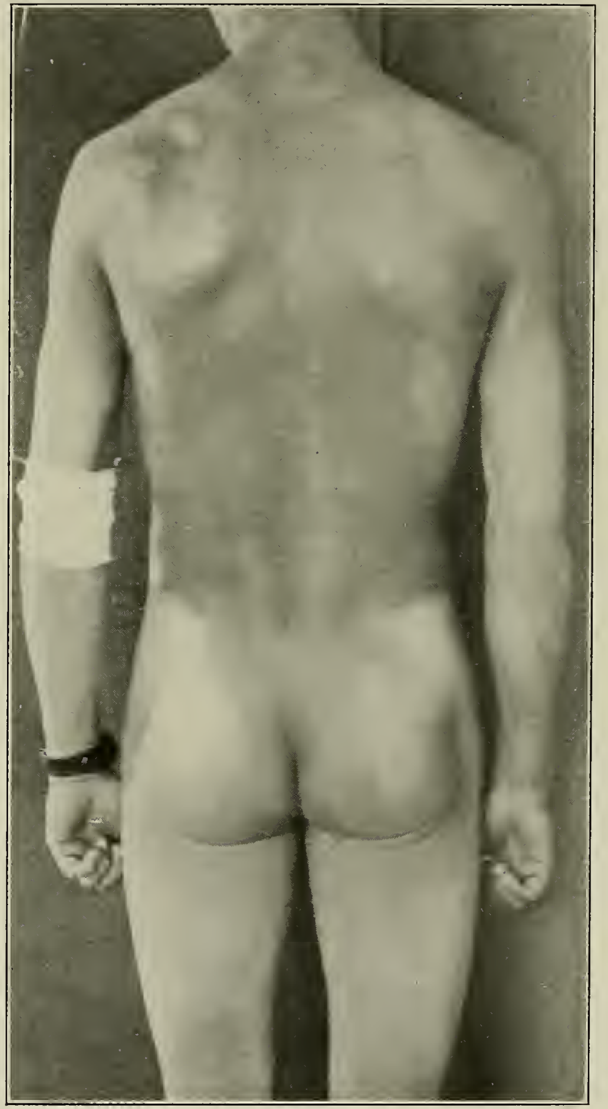

Fig. 41.—Rear view of same patient shown in Fig. 40.

Case II.—Private M. Exposed to the same strong concentration of mustard gas one-half hour in one shift. Thirty minutes after the end of the exposure he became nauseated and his eyes were irritated and burned. He took the routine kerosene rub and showers, but soon developed severe photophobia with symptoms of shock. Within a few hours entire body was erythematous. Vesication and desquamation began on the second day. When seen one week after the exposure his skin showed a general erythema and pigmentation except where protected by his rubber gloves, rubber boots, and belt. The skin of the neck was almost black; the horny layer had completely desquamated. Pigmentation was very marked over the forearms, hands and belly, increasing toward the pubic region. The part of the face protected by the gas mask contrasted markedly with the deep black pigmentation outside of the borders of the mask. The back was erythematous and desquamating. The skin of the small of the back was almost black, except for the white belt line running across it. The buttocks showed intense erythema and desquamation. In the right gluteal fold there was an area of deeper necrosis. In the axillæ, at the bends of the elbows, and around the genitals there were deep necrotic areas, exuding pus and giving off an odor of putrefaction. There was deep necrosis of the glans penis, of the scrotal skin and of the contact surfaces of the genitals and skin of left thigh. There was a bilateral inguinal adenitis. There were numerous small pustules over the forearms and lower portion of the back.

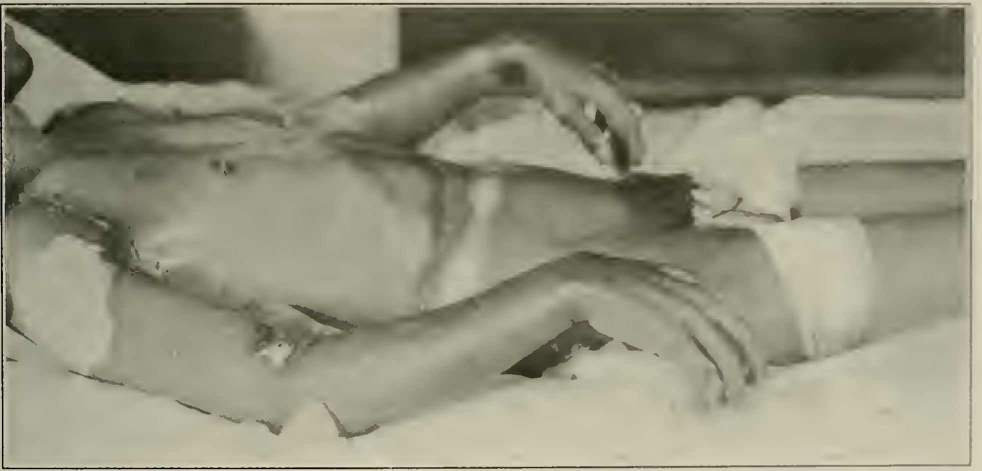

Fig. 42.—Photograph one week after one-half hour exposure to strong concentration of mustard gas. During this time treated by the grease method. Photograph shows very well the protection afforded by the tight belt. The more marked lesions in the axillae, bends of the elbows, and genitals and the large flaky character of the primary desquamation and the pigmentation are well shown.

Case III.—Private H. Exposed ten to twelve minutes in one shift to the same concentration of mustard gas as the above cases. First symptom was burning of the eyes; later mild shock, with vomiting; soreness of the throat and coryza. By the next morning had slight erythema over the body most marked about the genitals. Vesication began on second day. When seen one week after exposure the face showed some pigmentation which was more marked in the neck, and the skin of the face and neck showed areas of desquamation with erythematous bases. The back was mottled with pigmented areas. Low on back the areas became confluent. Across the small of the back there was a sharply demarcated area which was protected by the belt. Over the pigmented areas there were flakes of desquamated epithelium. When these were removed an erythematous base appeared. The skin of the axillæ was very erythematous with areas of deep necrosis in the creases where the hair was thickest. There were also areas of deep necrosis in the bends of the elbows. Pigmented bands were present in the groin parallel with Poupart's ligament. The skin of the penis was erythematous without necrosis. The skin of the scrotum was necrotic throughout with an odor of putrefaction. Areas of necrosis were present in the crotch. The buttocks were erythematous, pigmented and desquamating. There were areas of necrosis about the anus. The skin of the popliteal spaces showed erythema, desquamation and slight necrosis. (See Figs. 40 and 41.)

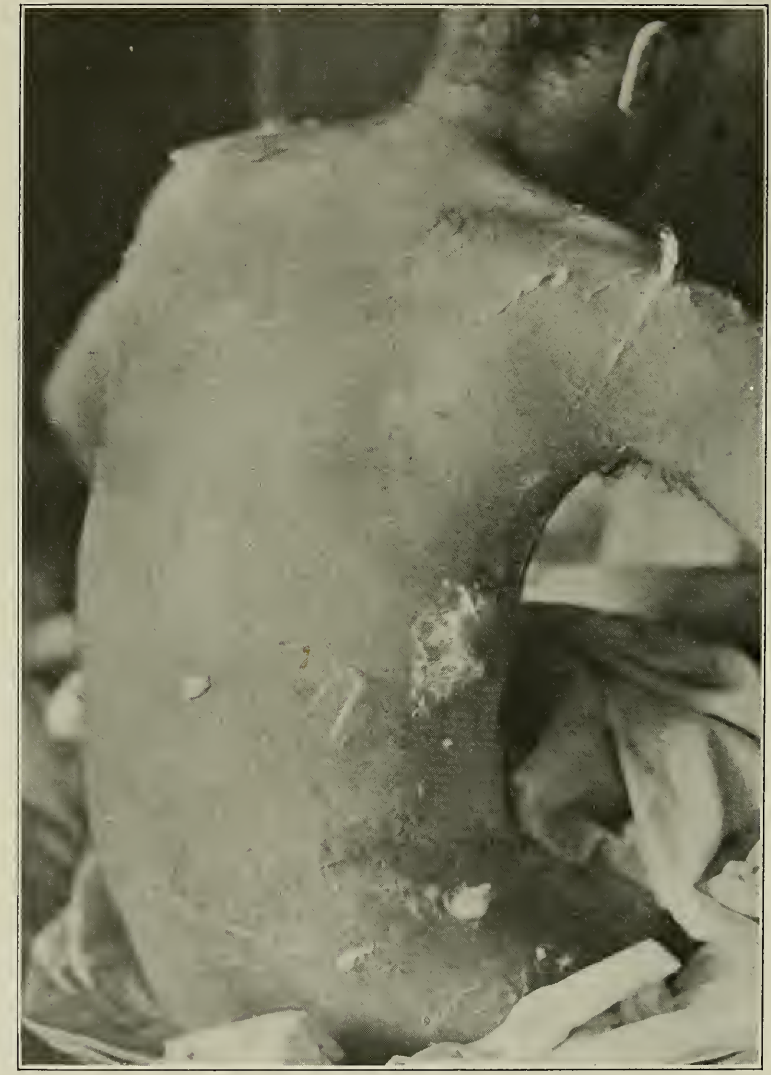

Fig. 43.—Back of same patient as the preceding figure.

Case IV.—Private E. Exposed ten to twelve minutes in one shift at the same concentration as the others. He claimed to be especially susceptible to mustard gas because he had had frequent burns previously from slight exposures.

He first noted irritation of the eyes and found that his left arm was red to the elbow. He took an American oil rub, after which he developed a general erythema. Vesication began on the second day. When seen a week later, the skin showed a general pigmentation except where protected by the gloves, boots, and gas mask. The pigmentation was the most marked over the face, thorax, and

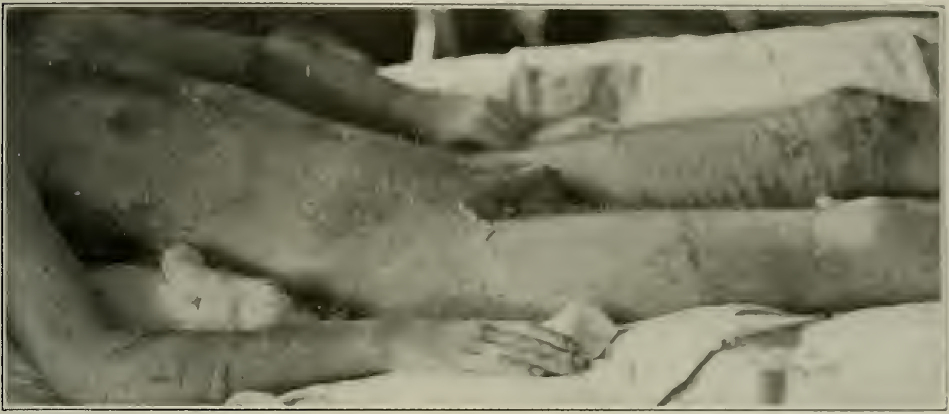

Fig. 44.—Photograph one week after three-quarters hour exposure to strong concentration of mustard gas. Treated twelve days with grease method with resulting severe gangrene of the epidermis and large decubitus from which he died three weeks later.

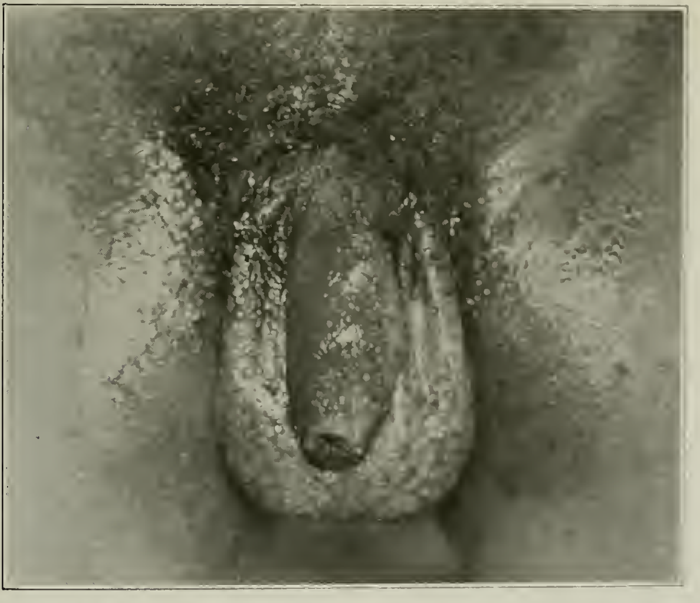

Fig. 45.—Genitals two weeks after exposure to mustard gas vapor. During this time treatment was of the ordinary grease method and resulted in secondary infection, deep necrosis and phimosis. This photograph shows especially well the deep follicular abscesses in the skin of the scrotum and penis.

abdomen. The back was erythematous with large areas of collapsed vesicles over the scapulæ. The axillæ were erythematous, the skin desquamated with deeper necrosis where the hairs were thickest in the folds. The deepest necroses on the upper part of the body were in the bends of the elbows. Wherever the skin had been rubbed over the bony prominences, there were thick crusts of dead skin. Over the buttocks and the inner surface of the left thigh where the scrotum was in contact the skin was markedly erythematous with desquamated epidermis. Over the right trochanter there was a large blister. There was a fine branny desquamation over the entire body. The penis was markedly edematous and phimosed with pus exuding from the meatus. The skin of the scrotum was completely necrosed and exfoliated. In the hair follicles there were numerous pustules. There were also small pustules over the forearms, shoulders, and back. Axillary lymph glands were enlarged. This patient had old mustard burn scars on his face, arms and feet. (See Figs. 146 and 147.)

Case V.—Private W. Exposed one-half hour in two or three shifts. Same concentration as in other cases. On coming from work he felt slightly ill and after eating supper was nauseated and vomited. He became very pale and showed severe shock. His throat was dry and sore and voice impaired. He had worn gas mask, rubber gloves, and rubber boots. He had also had mustard gas burns of the hands previously. Showed general erythema a few hours after exposure. Vesication began on second day. When seen a week after exposure he was still in a state of severe shock and presented the signs of a diffuse bronchopneumonia. At this time his skin showed a generalized necrosis over the back, axillæ, chest, arms, abdomen, buttocks, groins, thighs, and popliteal spaces. The skin of the back exuded pus and there was a marked odor of gangrene over the entire surface, especially over the back. The chest and neck were deeply pigmented and the epidermis had exfoliated. Large patches of exfoliation were present over the chest and shoulders. The abdomen showed a marked line of

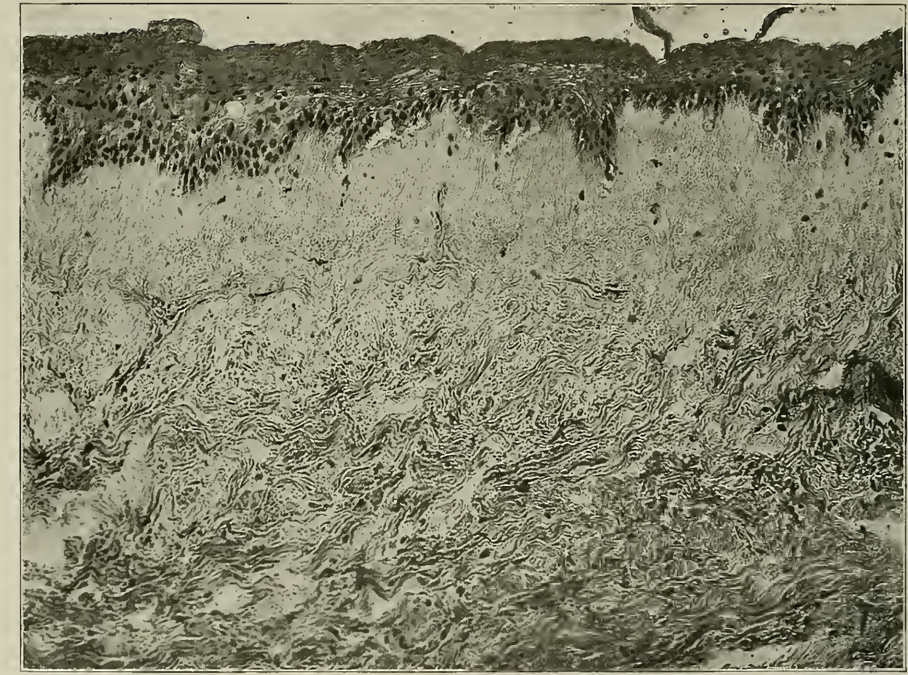

Fig. 46.—Human skin one week after exposure to strong concentration of mustard gas vapor with resulting erythema followed by pigmentation. No vesication. Microscopically, the changes consist of increased cornification, pyknosis of the cells of the epidermis and necrosis of the papillary layer of the corium. The only living cells in the upper portion of the corium are pigmented chromatophores.

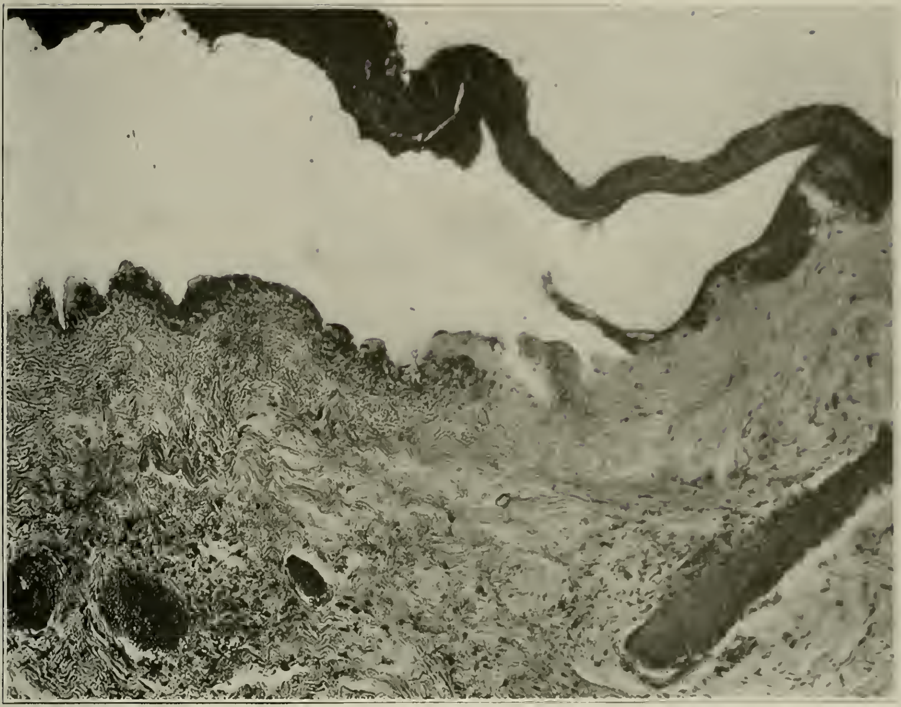

Fig. 47.—Human skin from Case II, one week after exposure to strong concentration of mustard gas vapor. Edge of large vesicle, showing the necrosis of the upper portion of the corium, congestion of vessels and separation of the epidermis.

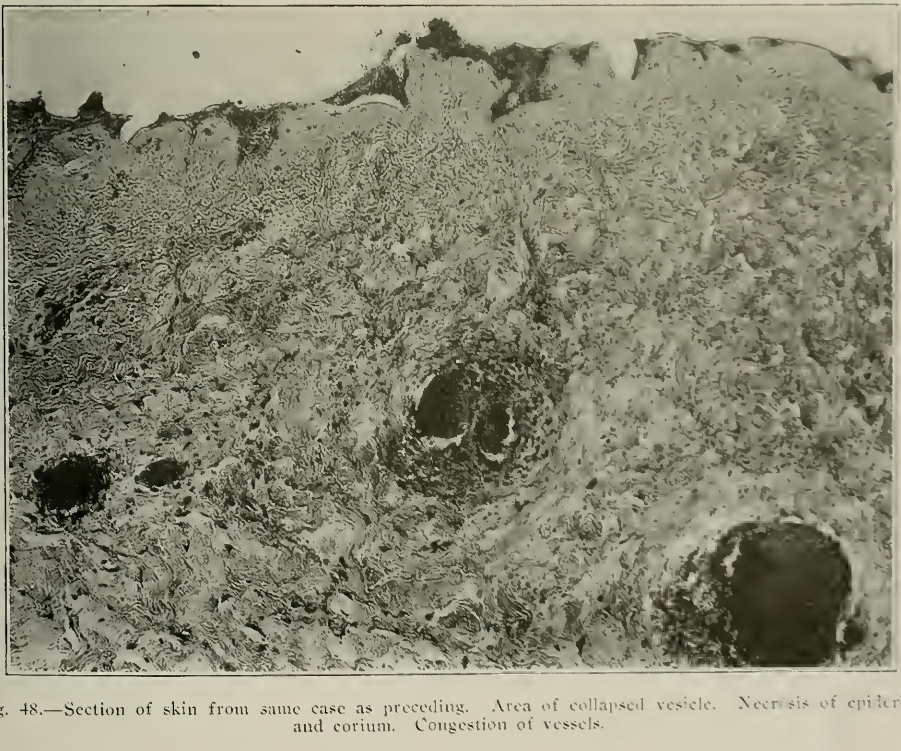

Fig. 48.—Section of skin from same case as preceding. Area of collapsed vesicle. Necrosis of epidermis and corium. Congestion of vessels.

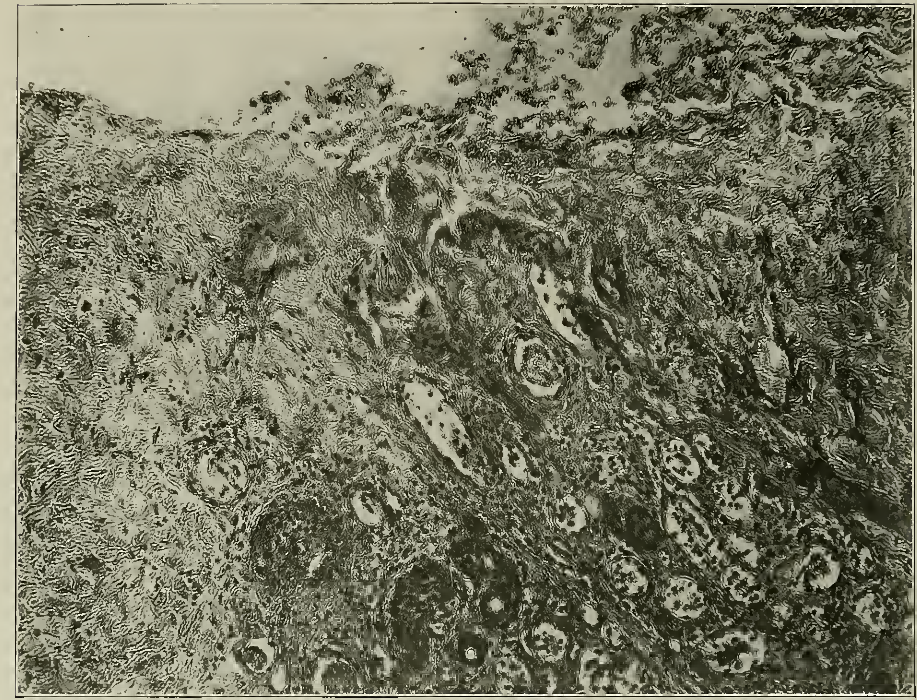

Fig. 49.—Skin from axilla of same patient as preceding. Necrosis of skin to the depth of the large sweat glands. These show also partial necrosis with some early regeneration.

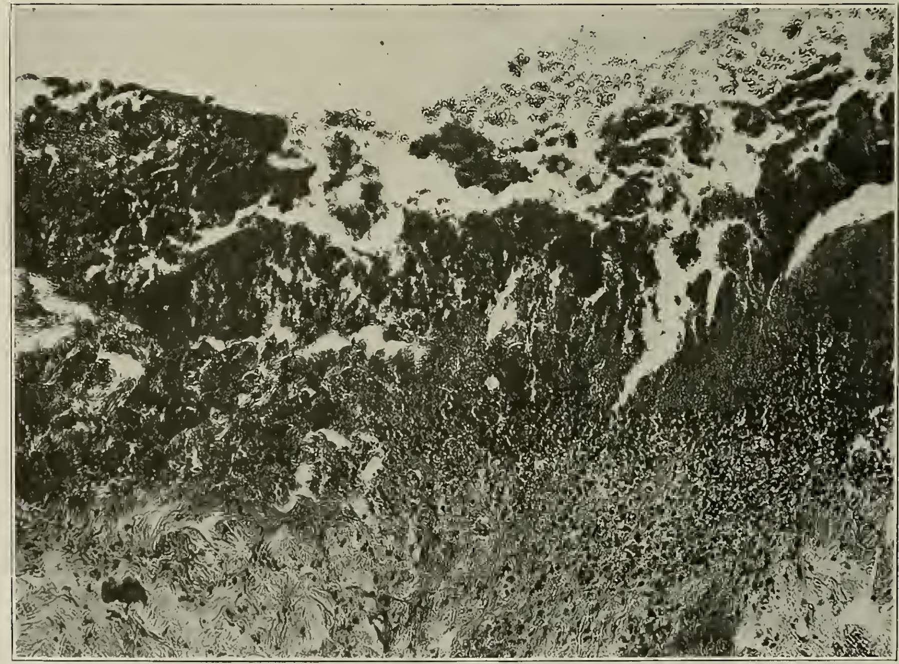

Fig. 50.—Infected gangrenous area from skin of back of same patient as preceding.

demarcation corresponding to his belt. Everywhere a foul pus exuded from the necrotic surfaces. The genitals showed complete necrosis of the skin of the penis and scrotum, the surface being covered with a greenish-gray slough with numerous miliary abscesses corresponding to the hair follicles. The axillæ, buttocks and popliteal spaces showed the deepest necrosis. The portion of the face covered by the gas mask showed a milder lesion. For several weeks this patient was at the point of death, but after changing the method of treatment from the grease to the Dakin's solution the infection was finally conquered and regeneration slowly took place. When seen several months afterwards, the patient was engaged in office work and his skin showed extensive areas of cicatrization resembling those of severe thermal burns. (See Figs. 42 and 43.)

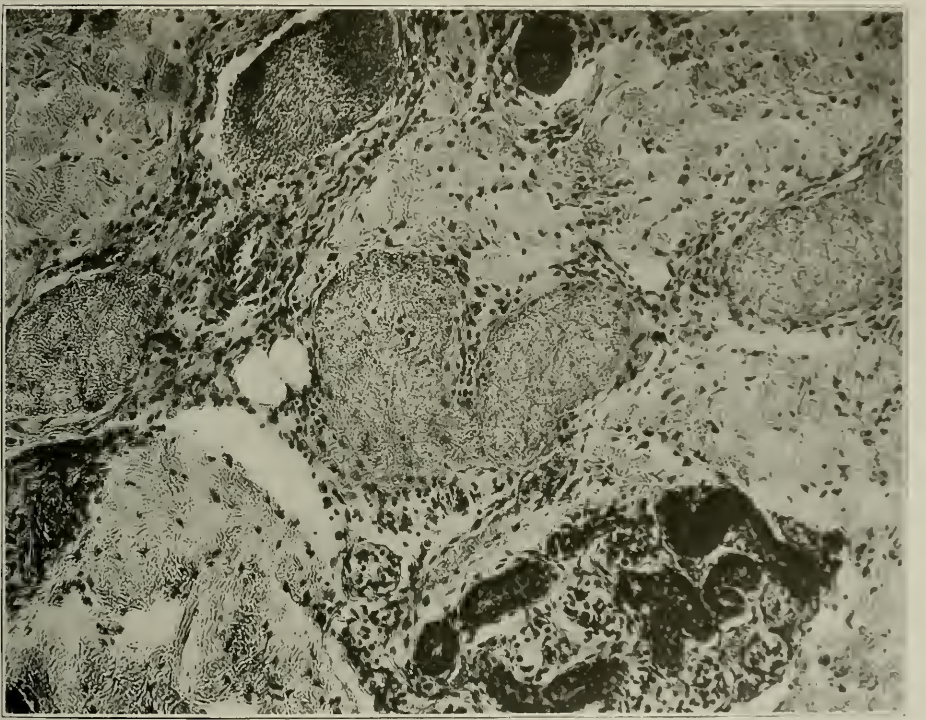

Fig. 51.—Section of corium from skin of same patient as preceding showing dilated lymphatics filled with fibrin thrombi, in the lower portion of the corium. Some of these lymphatics contain partially hemolyzed red blood cells in small numbers.

Case VI.—Private Ha. Exposed one hour in two or three shifts at the same concentration. Almost immediately he became nauseated, pale, and vomited. He took a hot bath and kerosene rub, but quickly developed symptoms of severe shock. He vomited violently, had a severe diarrhea and extreme thirst. His face was very pale but his body was very red. Two days later large vesicles developed over the back, chest, legs, and genitals. A condition of severe shock persisted. On the fourth day his temperature began to rise and an odor of putrefaction was noticed for the first time. The epidermis over his whole back was said to have been rubbed off at this time. By the fifth day the skin was discharging pus over the back, the patient became delirious, the pulse was rapid and thready and the gangrenous condition of the skin increased. Death took place on the eleventh day and a description of his skin changes is given in full in the Autopsy Protocol on page 169 of Chapter V. (See Figs. 47 to 51, and 130.)

Case VII.—Private S. Exposed three-quarters of an hour in two or three shifts to the same concentration. On changing his clothes, he noticed that his head, face and neck were very red except where the mask had covered the skin. He took the kerosene rub and bath but soon became nauseated and developed symptoms of severe shock. At the same time an intensely painful conjunctivitis and a severe irritation of the entire skin developed. During the next three days vesicles developed over the entire body. These were opened and

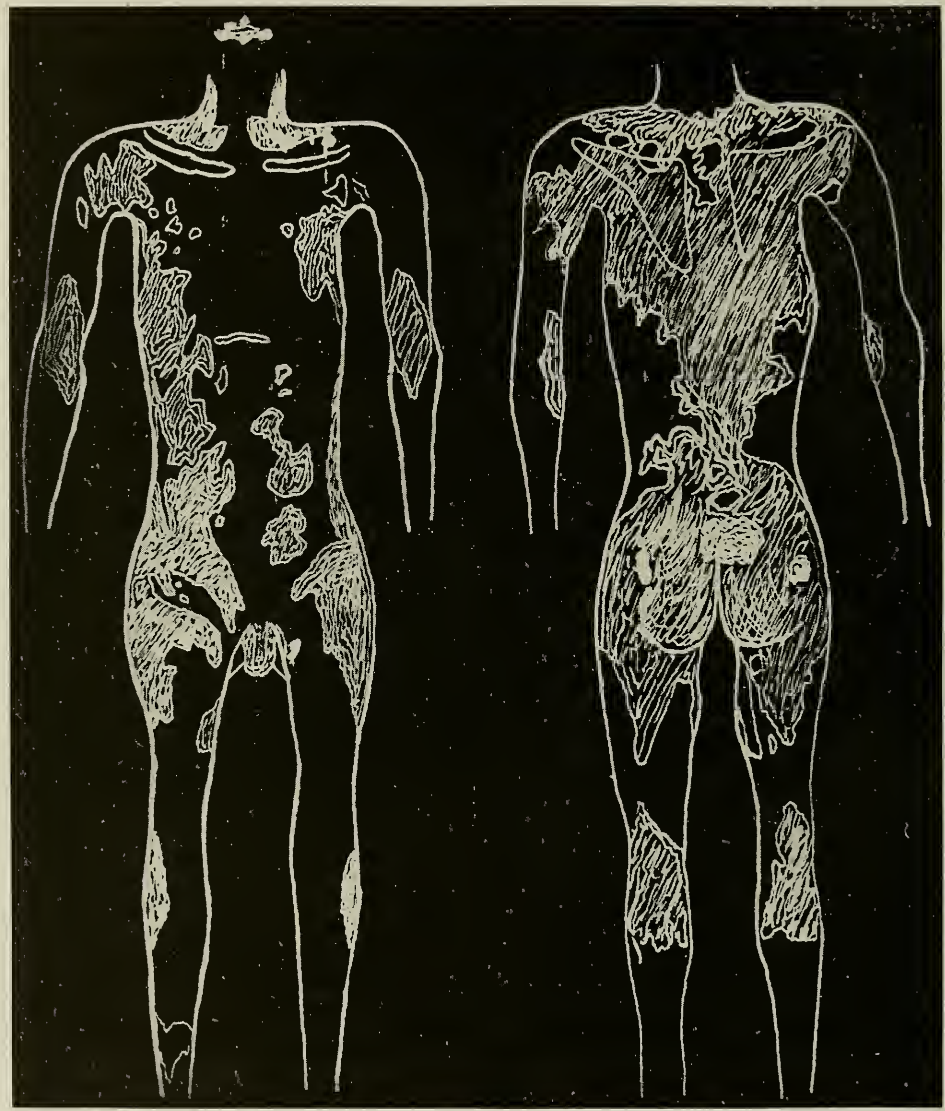

Fig. 52.—Case III. Diagram illustrating the distribution of mustard gas eschars, four weeks after exposure to strong concentration of mustard gas. The hatched areas represent the lesions.

drained. Temperature began to rise on the fourth day. On the sixth day there was marked exfoliation of the epidermis. When seen a week after the exposure his skin was gangrenous and infected throughout and his condition was very bad. With the change of treatment to the Dakin's sponge bath and reduction of the infection his condition improved somewhat. At one time it was thought that he was out of danger but his skin was almost completely exfoliated and large areas of decubitus developed over the back. Regeneration of the surface epithelium did not take place and with the increasing decubitus the patient died four weeks after the exposure. An autopsy was refused but a careful study was made of his skin and the localization of the lesions carefully determined, as in Fig. 52.

The nature of these lesions was as follows: The entire back showed a deep

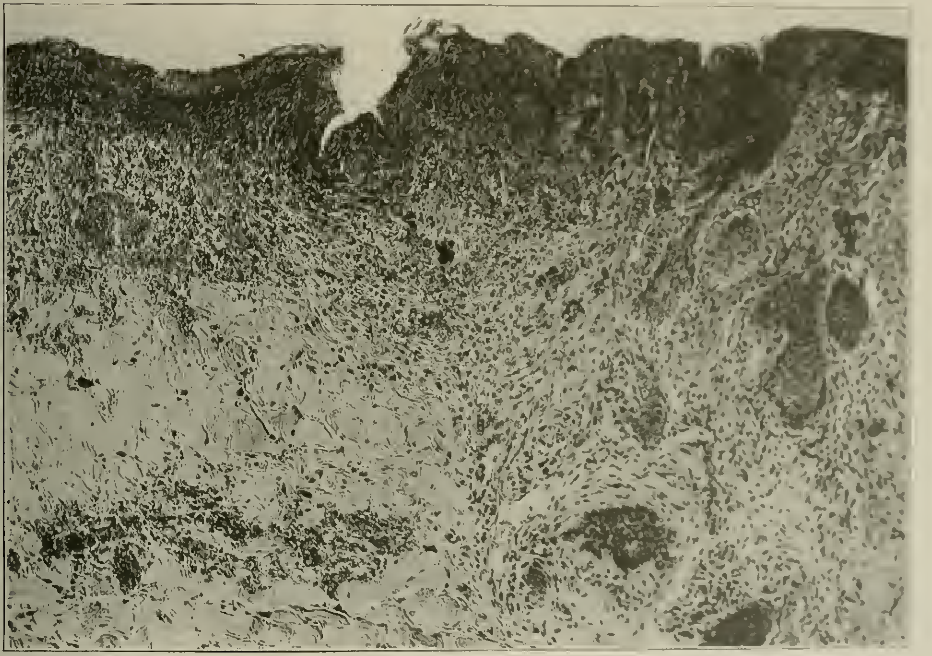

Fig. 53.—Microscopic section of mustard gas eschar from Case III. four weeks after exposure. Areas of regenerating epithelium from the sweat glands.

necrosis extending through the corium into the subcutaneous tissue in many places. In part, the necrotic surface was covered by a purulent exudate. Over the anterior surface of the body there were large irregular areas of deep necrosis, exuding pus. Between the areas of deep necrosis, the epidermis was completely lost, the denuded surface was congested and the capillary tufts in the papillæ of the epidermis could be easily seen. The portion of the face covered by the mask showed a deep erythema, pigmentation and desquamation, with areas of necrosis on the lips and at the angles of the mouth. The skin of the genitals was gangrenous and there was a foul odor of putrefaction. The surface was covered with a thick tenacious eschar, greenish-yellow or grayish in color. When this was removed, a purulent hemorrhagic base was exposed. Over the sacrum there was a large area of decubitus extending to the bone. (See Figs. 44 and 153.)

Microscopic examination of the necrotic skin showed a complete necrosis of the epidermis and corium, with secondary infection, the necrosis in many places extending through the corium to the subcutaneous tissues. No evidences of regeneration were seen in these areas of deepest necrosis but in those portions of the skin where the necrosis involved only the upper part of the corium areas of regenerating epithelium from the sweat glands were present. (See Fig. 53.) In the skin of the scrotum the regeneration of the hair follicles formed small solid masses of epithelium as large as a millet seed, which could be distinctly seen and felt through the skin. These had been regarded as follicular abscesses but microscopic examination showed them to be regenerative areas of squamous epithelium.

Summary of Cases

These seven cases constituted the only examples of severe general gassing seen by us, but they were said by an army officer, returned from the other side, to be more severe than any he had seen in France or Belgium. In addition to these cases, about seventy cases of local mustard gas lesions of the skin of varying degrees, both in acute and chronic stages, and presenting a great variety of clinical pictures were seen by us. As the result of our observations on these cases we are led to the following conclusions:

1. Even after slight mustard gas erythemas, particularly when these have been several times repeated, there develops a dry, desquamative eczema or dermatitis, particularly between the fingers and on the genitals, which may be mistaken for itch. This chronic lesion, otherwise trifling, is especially annoying for its constant itching. The genital lesions may be mistaken for venereal affections.

2. Slight mustard gas lesions, not proceeding beyond the stages of erythema and pigmentation, may often be made to vesicate by slight trauma, such as rubbing, pressure or by being struck. This phenomenon, which is analogous to Nikolsky's sign has been misinterpreted as indicating a persistence of the mustard gas in the injured area with secondary action, or as a delayed reaction. In our opinion this is due entirely to the lowered vitality or partial necrosis of the papillary layer of the dermis with the epidermis adherent so that relatively slight injuries cause the epidermis to separate and form a vesicle.

3. It has been stated that the fluid of a mustard gas vesicle when applied to uninjured areas of the epidermis will produce fresh lesions. This is not true. The fluid of these vesicles is absolutely without action upon either the skin or conjunctiva.

4. No specific susceptibility to mustard gas lesions of the skin is acquired by repeated exposures. Healed mustard gas lesions, like all other healed lesions, have a lower degree of vitality and are more susceptible to all forms of injury.

Summary

1. Dichlorethylsulphide (mustard gas) is an escharotic, specific in its action upon the epidermis and tissues of corium, particularly upon the endothelium of the vessels. The lesion may vary according to the concentration and period of exposure, presenting either a hyperemia, vesicle, or eschar.

2. The lesion is a chemical burn unlike that produced by heat, electricity, or the ordinary corrosives such as sulphuric, nitric, and hydrochloric acids or

strong alkalies. Of all these agents, the effects are most closely allied to those of hydrochloric acid, but are much greater in intensity. It differs from a heat burn in the absence of thrombosis, in the greater degree of fluid exudation, in the greater moistness of the affected area and in the fact that the necrosis as shown by the loss of nuclei requires hours, or even days, for its complete development. The coagulated, shrunken and cooked appearance of the tissues in heat burns is not apparent in the tissues of mustard gas burns.

3. The vessels in the affected area are severely damaged and collapsed and there is a local anemia in the earlier stages, with a marked fluid exudation and leucocyte migration. The process is nonhemorrhagic and nonthrombosing.

4. In clinical cases of general gassing with mustard gas, the skin is at first pale, then becomes erythematous within a few hours. With the development of the erythema there is usually intense shock with extreme nausea and vomiting. Vesication begins usually on the second day and progresses for several days, eschar formation appearing on the sixth or seventh day. The temperature usually does not rise until the development of escharization and secondary infection.

5. In man the necrosis of the epidermis is usually evident, microscopically, in two hours through the hydropic change in the epithelium and early vesicle formation. There is no deep edema. It is confined to the epidermis and to the papillary layer in the early stages.

6. In animals the intense and deep edema is most striking and altogether different from that seen in man. Vesicle formation was not noted by us in animals. The fluid from vesicles has no irritating property and can produce no secondary lesions.

7. The deep penetration of the smallest quantities applied to the surface is a most striking feature. There is an undoubted entrance through the hair follicles, sebaceous and sweat glands.

8. The slowly progressive development of the necrosis is a specific characteristic, the height of the necrosis being reached five to ten days after application. In this respect also there is a similarity to the x-ray burn. This may, in part, be explained by contraction and death of the vessels with resulting anemia in the affected area.

9. The painlessness of the lesion is also a marked characteristic. This may be explained by the edema and degeneration of the nerve endings in the affected portion.

10. Areas of the skin damaged by mustard gas may not show vesication or exfoliation unless they are subjected to pressure or rubbing. Slight trauma upon such damaged areas may produce vesicles or blebs some time after exposure. This phenomenon is analogous to Nikolsky's sign in pemphigus.

11. In none of our animals, and in none of our clinical cases, was there any conjunctivitis or irritation of the respiratory tract produced by local cutaneous applications. We conclude that there is no evidence of metastasis from the local lesion as claimed by both Meyer and Haldane. We believe that the conjunctival and respiratory lesions are due alone to the direct action of mustard gas and when animals are protected from the vapor no lesions in these organs will result, no matter how severe the skin burn.

12. Contrary to the statements of certain English and French observers, the admixture of water does not increase the escharotic action, but if the oil is immediately washed away, the lesion is greatly reduced in intensity. Washing within two minutes with tincture of green soap may entirely prevent the lesion or result in only a slight hyperemia.

13. We believe that the lesions observed in the axillæ, between the fingers and toes, around the genitals and between the thighs of men gassed in action are probably due to the greater moisture of these parts from perspiration and the resulting re-solution of the gas, as well as to the more abundant gland supply of these parts.

14. The slow healing is probably chiefly due to the vessel injury and the relatively slight leucocytic demarcating infiltration. In this respect the lesion is strikingly like an x-ray burn of the skin. Regeneration of the epidermis, after complete necrosis, takes place from the epithelium of the sebaceous and sweat glands. Marked pigmentation may persist for long periods. This pigmentation is due to the formation of many pigmented chromatophores in the upper portion of the corium. These findings present positive evidence for the production of melanin by connective-tissue and endothelial cells. Chronic eczema with desquamation and intense itching is a frequent sequel to repeated slight mustard gas burns.

BIBLIOGRAPHY

[1] MEYER, VICTOR: Ber. d. deutsch. chem. Gesellsch., 1886, xix, No. 3, 3259.
[2] MEYER, VICTOR: Ber. d. deutsch. chem. Gesellsch., 1887, xx, No. 2, 1729.
[3] GIRAUD, ALBERT: Jour. de méd. et de chir. prat., Nov. 25, 1917, lxxxviii, 890-895.
[4] TEULIÉRES: Jour. de méd. de Bordeaux, Nov., 1917, No. 12, p. 247.
[5] MANDEL AND GIBSON: Jour. Am. Med. Assn., Dec., 1917, lxix, p. 1970.
[6] HALDANE: British War Reports.
[7] KOLLS AND GILBERT: British War Reports; British Medical Reports.
[8] RAPER AND BALL: Ibid.
[9] MARSHALL AND MILLER: Chemical Warfare Service Reports.
[10] KOLLS AND GILBERT: British War Reports.
[11] Ibid.
[12] MACKENZIE: Ibid.
[13] HALDANE: Ibid.
[14] MCNEE: Ibid.
[15] MCLEOD: Ibid.
[16] DUNN: Ibid.

CHAPTER III

THE OCULAR LESIONS PRODUCED BY DICHLORETHYLSULPHIDE ("MUSTARD GAS")

Since conjunctival irritation is so prominent a feature of the use in warfare of dichlorethylsulphide ("mustard gas"), the first clinical reports of the effects of this gas emphasized particularly its action on the eyes. These earlier reports speak of the early development (six to twelve hours) of a conjunctivitis in practically all of the men exposed to the gas. The eye-symptoms may appear first, or at the same time with the cutaneous burns. The conjunctivæ are described as congested, the lids very much swollen, with moderate lacrimation, vision not affected in any marked degree, and recovery usually prompt in all the mild cases. These scattered clinical observations are all very superficial, and no thorough studies of the ocular lesions produced by mustard gas are available in the general literature. The best reports are the following, drawn from French and Italian articles.

Giraud (*Journal de Médecine et de Chirurgie Pratiques*, 1917, lxxxviii, 890), in describing the clinical symptoms of mustard gassing, groups the eye lesions as one of the three cardinal groups of symptoms produced by the gas. He describes these symptoms as essentially congestive. The conjunctival vessels appeared sinuous, dilated, often of a bright red color; and at times in the areas of the finest ramifications of these vessels, at the points of confluence, there occurred small red "lakes," the size of a lentil. No blisters or ulcerated lesions were noted in the early stages. Pain, as a rule, was quite moderate or absent, although severe in certain cases. Lacrimation was moderate. Impairment of vision was exceptional. Pupil reflexes were normal. In some cases the swelling of the eyelids was so marked as to occlude the eye completely. About 10 per cent of the cases seen were characterized by the most intense and diffuse congestion. These cases were evacuated. The lighter and moderate cases usually healed in two to three days. Treatment consisted in the use of a solution of soda bicarbonate in strength of thirty parts per thousand.

Teulières (*Journal de Médecine de Bordeaux*, November, 1917, lxxxviii; February, 1918, lxxxix), and *Teulières and Valois* (*Archives D' Ophtalmologie*, 1916-17, xxxv, p. 403) make the first detailed clinical observations on the ocular lesions produced by mustard gas. The great majority of the large number of cases observed presented eye symptoms that were benign and of short duration. Only a small number showed such serious lesions as to make it necessary to send them to a special service for observation. In fifteen hundred cases seen there was but one case of panophthalmitis, and three cases of ulceration of the cornea. In general the symptoms, particularly the photophobia, begin to improve within four to five days, and healing may be complete in two to three weeks. A few cases were seen in which the blepharoconjunctival irritation persisted for a longer time. A detailed description of one of these more severe cases is given. The lids of the right eye, especially the upper, were much swollen and opened with difficulty. Conjunctivæ in the cul-de-sac and in the palpebral portions very hyperemic; on the bulbar portion it was pearly white, porcelain-like, especially in the upper portion, where there was a hard collar of edema. Small punctiform hemorrhages were numerous, and there was a fine deep arborization of the pericorneal vascular plexus. The cornea appeared slightly granular, and no erosion could be demonstrated by the fluorescein method. The iris was congested, but no iritis was present, and no lesions were demonstrable in the interior of the eyeball. Ocular tension normal, ocular movements made difficult by the rigidity of the conjunctiva. Visual acuity, one-tenth. The left eye showed similar changes to a less degree, and without the collar of edema. Vision, ten-tenths. Symptoms were: intense photophobia, continuous lacrimation, smarting and sensation of burning, heaviness of lids, and small amount of yellowish mucopus in the inner angles. Treatment consisted of warm vaporization and the instillation of a collyrium of atropine, and iodoform ointment. The condition, however, resisted treatment.

In the later paper, *Teulières* and *Valois,* the ocular symptoms are described in fuller detail, as follows: Blepharitis, conjunctivitis, chemosis, edema of lids, congestion of iris, symptoms suggesting a slight iritis, cloudiness of the papilla, slaty tint of the retina (edema?), benign neuroretinitis, congestion of the retinal veins, with diminution of visual acuity. They advance several hypotheses in explanation of the lesions of the posterior segment; (1) that they are secondary to the inflammation of the anterior segment; (2) that the inflammation is an extension through the sinuses and optic meninges, producing a retrobulbar neuritis that may or may not extend as far as the papilla. The lesions of the anterior segment always terminate in healing, and their knowledge of the neuroretinitis cases was too slight to make definite prognosis possible for such cases, although they maintain that both the superficial and deep ocular lesions due to toxic gases are essentially benign. Their treatment consists of warm vapor baths for the eyes, lasting ten minutes, and repeated four to five times daily; instillations of adrenalin and cocaine for the pain, frequent instillations of atropine for the iris phenomena, and in the cases with neuroretinitis, blood-letting from the temple and mercurial rubs upon the forehead.

Pissarello (*Giornale di Medicine Militare,* 1918, lxvii, 128) describes the ocular conditions caused by "yprite" (mustard gas). He divides the cases into the light and the moderately grave forms.

The light cases develop five to ten hours after gassing, with headache, burning in the eyes, lacrimation, marked photophobia, swollen eyelids, congested conjunctivæ, the bulbar conjunctiva hyperemic in area corresponding to palpebral fissure. Pericorneal injection absent or slight; pupils negative. Symptoms begin to decline in twenty-four to thirty-six hours.

In the severe cases all symptoms more marked, after a shorter incubation period. Eyelids swollen, heavy, "pin prick" pains in eyes; cul-de-sac reddened, chemosis of bulbar conjunctiva, punctiform conjunctival hemorrhages; cornea usually clean and transparent, in some cases showed desquamation of epithelium. In two cases in which cocaine had been used and a binocular bandage pressed lightly upon the eyes corneal erosions were present. Anterior strata of cornea turbid in some cases due to very minute, grayish white dots. Sometimes this turbidity shows as a grayish white line running horizontally across lower half of cornea. Usually after three to four days there is a remission of the ocular condition. Ulcers, when present, heal rapidly. The pupil, formerly contracted, dilates readily under atropine. As an exceptional condition cicatricial ectropion was observed. Ophthalmoscopic examination showed in 20 per cent of the graver cases a slight hyperemia of the papilla, with slight tortuosity of the retinal veins. When cases were dismissed there was no disturbance of visual field or visual acuity. He concludes that the ocular lesions are relatively benign. The ocular syndrome reminds him of snow blindness and electric ophthalmia. He believes that the ocular lesions are due to the direct action of the gas and not to any toxic substance in the blood; and conducted a number of experiments, using instillations of tears and sweat from injured soldiers into the conjunctivæ of rabbits, without results. He considers the presence of bulbar chemosis of importance in judging seriousness of cases. As methods of treatment he advises avoidance of bandages and cocaine; and advocates the use of an eye wash of 2 per cent bicarbonate or sterile water, with hot vapor fomentations, and a zinc oxide pomade for the lid lesions.

Canelli (*Rivista Ospedaliera,* 1918, viii, 2) describes a fatal case, with autopsy, of poisoning by "yprite" (mustard gas). The eyes presented a diffuse bilateral conjunctivitis, without exophthalmus. No microscopic examination made.

These are the only clinical descriptions available in the general literature; and it is worthy of note that no pathologic studies have as yet been published. In spite of the fact that Victor Meyer, the discoverer of mustard gas, noted the conjunctival lesions in man and in experimental animals the literature contains no reports of further investigations in this direction. The material presented by us below must therefore be regarded as opening up a new field in ophthalmic pathology.

EXPERIMENTAL DICHLORETHYLSULPHIDE LESIONS OF THE EYE

Method of Application.—Application of dichlorethylsulphide to the conjunctiva was made in two ways. In order to secure results comparable to those obtained by direct application to the skin, as previously reported, an extensive series of animals was made use of, in which the liquid dichlorethylsulphide was applied directly to the center of the cornea by means of a fine pipette in uniform minute droplets determined to be about 0.0004 c.c. in size. The animal's lids were at once released and by its blinking the mustard gas liquid was spread in the conjunctival sac. By using a uniform height of column of dichlorethylsulphide in the pipette the effort to maintain a standard size of droplet was quite successful. However, we realize that slight variations in the amount applied are unavoidable. In another series, the animals were exposed to dichlorethylsulphide vapor in varying concentrations and for varying times in a respiration chamber especially devised for the purpose (see p. 131). Both pure and crude forms of mustard gas were employed.

I. Symptoms and Gross Pathology

Although the objective symptomatology and gross pathology of the lesions produced by direct application of the liquid mustard gas and by exposure to the vapor are essentially similar in the two cases, there are slight differences depending entirely upon method of administration which make it desirable to consider them separately.

Direct Application

The Rabbit.—*At once,* upon application of a standard droplet (.0004 c.c.) of dichlorethylsulphide to the center of the cornea, the rabbit blinks repeatedly but shows no other evidence of irritation for one or two minutes when there is usually a period of rapid blinking and rubbing of the eye with the fore paws. At the same time there is a definite increase in lacrimation, but not to the point of epiphora. When at rest the eye may be held partly closed. Thereafter the rabbit shows but slight signs of irritation throughout the earlier stages, except that at long intervals the eye and nose may be rubbed with the paws; the affected eye is not opened as widely as the other and lacrimation is moderately increased. *Fifteen minutes* after application there is beginning congestion of the vessels of the superior palpebral conjunctiva. At the same time there may be a slight decrease in the normal luster of the eye. The fluorescein test is positive as early as ten minutes. (See paragraph below on fluorescein tests.) *Thirty minutes* after application there is increased lacrimation and the congestion of the palpebral conjunctival vessels may now be so marked that there is a pinkish reflex through the upper lid. These changes gradually increase during the next half hour.

At one hour the first evidences of edema appear in the form of localized thickenings of the conjunctiva about 1 mm. in diameter. These occur most frequently in the superior palpebral conjunctiva near the fornix and at the upper border of the nictitating membrane. These areas are so small and so translucent that they can scarcely be seen except with the aid of the loupe and electric illumination. From *the second to the sixth hour* there is a progressive increase in the conjunctival edema, the localized edematous thickenings extending and coalescing until the ring of swollen edematous conjunctiva so encroaches upon the palpebral fissure that the sclera can not be made visible even by forced separation of the lids. The conjunctiva of the nictitating membrane shares in a marked degree in the formation of this edematous ring. The bulbar conjunctiva also shows a well marked edema, a definite chemosis being noted about the fifth hour. Between the fifth and sixth hours after application the cornea begins to show a faint clouding or haziness, especially in that portion of its lower half exposed in the palpebral fissure. The cornea is less lustrous than normal and when the surface is viewed under oblique illumination it is found to be somewhat roughened and irregular, indicating areas of destruction of the corneal epithelium. There is an increasing formation of seropurulent exudate. Photophobia gradually becomes more marked, the animal resisting all attempts to separate the lids. Lacrimation becomes excessive to the point of epiphora. The pupil reacts promptly to light.

From *the sixth to the twelfth hour* after application the edema of both palpebral and bulbar conjunctivæ continues to increase. There is now a very definite chemosis. At eight hours the clouding of the cornea has reached such a degree that it may be properly described as porcelain-like because of its bluish white opalescence. At this stage, likewise, there was noted an irregularly rounded area devoid of epithelium located in the mesial superior portion of the cornea. At ten hours the lids were found sealed by the accumulated seropurulent exudate along their margins. This adhesion of the lids, first noted at this stage, is a constant feature until the gradual subsidence of the acute inflammatory process about the third week. Very minute subconjunctival hemorrhages are likewise first noted about the tenth hour.

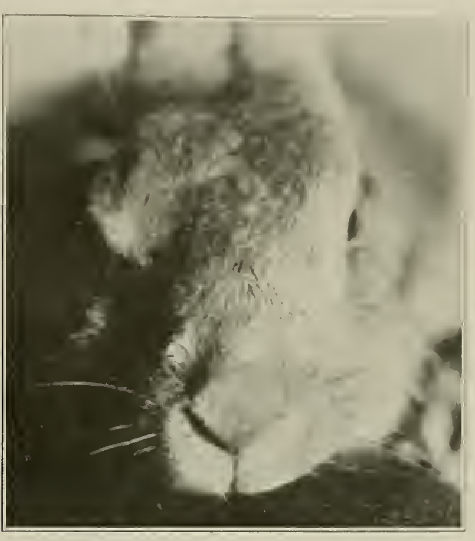

Fig. 54.—Twenty-four hours after direct application of standard droplet of dichlorethylsulphide to cornea of right eye. Marked edema of lids and surrounding subcutaneous tissue.

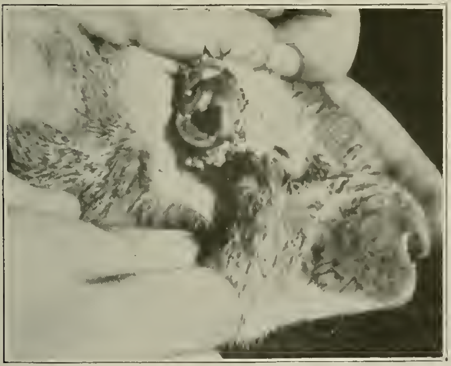

Fig. 55.—Twenty-four hours after direct application of standard droplet to cornea. Marked edema of lids, flecks of purulent exudate. The marked congestion of the conjunctival vessels is best seen in the bulging edematous mass of the superior palpebral conjunctiva.

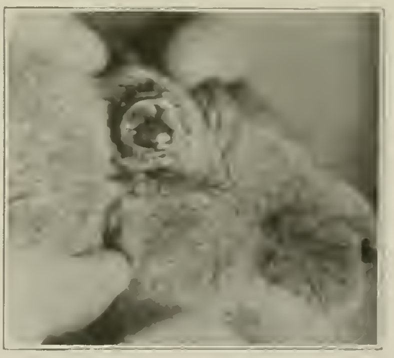

Fig. 56.—Twenty-four hours after direct application of standard droplet of crude mustard gas liquid to the cornea. Extreme edema of conjunctiva, especially marked in upper lid and nictitating membrane. Seropurulent exudate.

From *the twelfth to the twenty-fourth hour* the picture remains fairly constant. There is a gradual increase in the edema which spreads markedly into the periorbital tissues. (See Figs. 54, 55, 56.) The stiffened lids stand out widely from the eyeball and along the lid margins there is desquamation of the epithelium and other evidences of necrosis. The corneal opacity is still more marked and in some instances there is a purulent fluid in the anterior chamber. This hypopyon was never in great degree in this stage.

During *the second day* the edema remains so marked that the eye can not be thoroughly examined except by excision. Eyes thus examined at two hour intervals show a continuous progression in the lesion. The edema no longer continues to increase and in the thirty-six-hour specimens a definite decrease can be noted. In spite of this decrease the lids become even more indurated, indicating an increased cellular infiltration, and stand out far from the eyeball. The edges of the lids remain sealed unless forcibly separated and in the pocket thus formed thick purulent exudate accumulates. From the forty-four-hour stage on, this accumulation of thick purulent exudate becomes a very important feature. The denuded area upon the cornea increases in size and in practically all cases assumes a somewhat circular or elliptical form, occupying the greater part of the corneal surface but always approaching more nearly the inner quadrant of the limbus than the outer. The corneal opacity increases and frequently shows a curious distribution, similar to that which we have since learned has been described in human cases by Pissarello. This consists of a greater degree of opacity in the lower half of the cornea terminating in a more opaque band or zone running horizontally through the cornea just below its transverse diameter. This was best seen in a thirty-hour stage. The marginal lid changes become much more marked during this period.

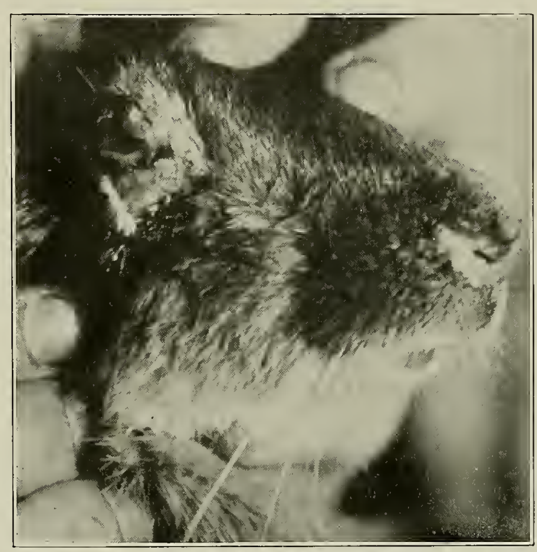

Fig. 57.—One week after direct application of standard droplet to the cornea. Lids still somewhat edematous. They were sealed by a marked purulent exudate which adheres along the lid margins and to the adjacent hair. A marked purulent rhinitis referable to involvement of the mucosa through the nasolacrimal duct, is evident.

The decrease in the edema continues through the *third* day but is noted especially in the palpebral conjunctiva, while the bulbar conjunctiva, in contrast, exhibits a chemosis which appears even more marked than hitherto.

The necrosis of the palpebral conjunctiva at the lid margins, and even of a zone on the dermal side of the lids becomes more evident, for now there appear numerous shallow ulcerations resulting from separation of the necrotic material.

On *the fourth day* the diminishing edema is followed by an increased congestion. More numerous and larger subconjunctival hemorrhages are frequently noted. These do not, however, occur either in such size or numbers as to permit the lesion to be characterized as hemorrhagic. The lids become increasingly sensitive to pressure so that the animals give evidence of pain when an attempt is made to separate them more widely. In the earlier stages the photophobia seemed to be the feature that gave the animal distress. The upper lid, near the inner canthus, begins to show a "kinking" or "ruffling" of the margin. This is a constant feature in the later stages. The marked seropurulent exudate persists.

There are no marked changes in the lesions during *the fifth day*. The seropurulent exudate is unchanged. The "ruffling" of the upper lid is more marked and the lids are still indurated and stand far out from the eyeball.

In rabbits that have been repeatedly examined, thereby separating the lids and removing the accumulations of purulent and necrotic material, the exudate is less in amount and more serous on *the sixth day*. In animals allowed to remain with the eyelids sealed for days at a time, the seropurulent exudate persists much longer and is, of course, much more destructive. At this time the necrotic lid hairs and the hairs of the face near the inner canthus begin to drop out resulting in some instances in an extensive depilation.

On *the seventh day* there are no marked changes from those previously described. The depilation about the inner canthus and over the lids is more complete and there is a beginning entropion of the upper lid which has the effect of drawing the stiff outstanding lid somewhat toward the eyeball. (See Fig. 57, a photograph of a rabbit showing the retardation in the course of the lesion when the lids remain sealed and the purulent exudate accumulates in the conjunctival sac.)

During *the second week*, the lids of eyes which have been frequently examined no longer become sealed between examinations, and the exudate decreases to a small amount of serous fluid carrying a few flakes of pus and necrotic tissue. The upper lid border comes to show a marked degree of "ruffling" or folding at the lid margin. This is accompanied by an irregularly distributed entropion. The lid margin itself becomes smooth, rounded and is devoid of lashes. The lower lid shows toward the end of the second week a marked ectropion with the same smooth rounded margin found on the upper lid. The periorbital depilation may be very extensive. The corneal opacity is unchanged. The normal corneal curvature may be distorted by small irregular staphyloma-like projections occurring most constantly inferiorly toward the inner canthus. However, these on section are found to be thickenings of the damaged cornea and not areas of bulging. Hypopyon may be present. (See Figs. 58, 59, 60.)

During *the third and subsequent weeks* the changes in the lesions are slowly progressive, demonstrating the sluggish character of the reparative process following injury with mustard gas. The "ruffling" of the upper lid border persists and gradually becomes more exaggerated up to the eighth week which terminates our period of observation. The ectropion of the lower lid also increases in degree, reaching in some cases an almost complete eversion. The margins of the lids are rounded, thickened, smooth and glossy, having the appearance of scar tissue. From the fourth week on there is a progressive vascularization of the injured cornea. As the newly formed vessels traverse the limbus the usual sharp differentiation between sclera and cornea becomes effaced. By the sixth week this process of organization becomes far advanced and the new formed vessels may be traced to the central region of the cornea as is clearly shown by Fig. 63. The organization is grossly most evident in that portion of the cornea which showed the primary

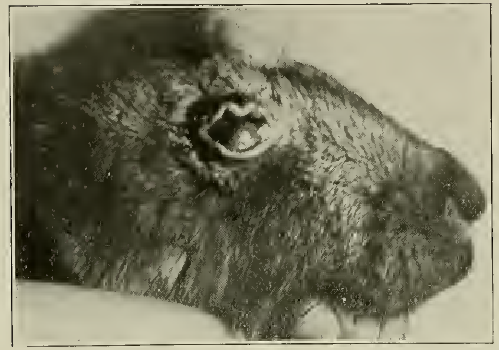

Fig. 58.—Two weeks after direct application of standard droplet to the cornea. Marked reduction of the edema. Much less purulent exudate. Indurated lids exhibit the characteristic "ruffling" and partial entropion of the upper lid in the later stages, and the smooth ectropion of the lower lid. The lower half of the cornea shows a marked clouding.

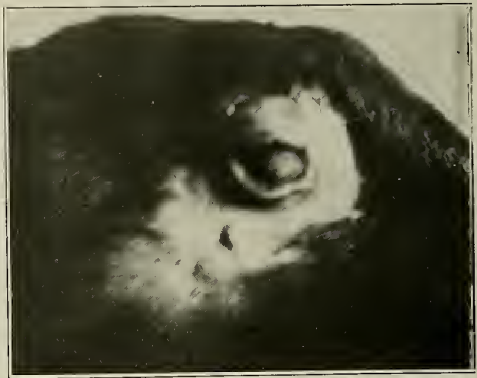

Fig. 59.—Two weeks after direct application of standard droplet to the cornea. Marked depilation about the eye. Characteristic "ruffling" and entropion of upper lid and marked ectropion of the lower. The corneal cloudiness and lack of luster are very apparent, likewise the apparent staphyloma in the lower half of the anterior quadrant.

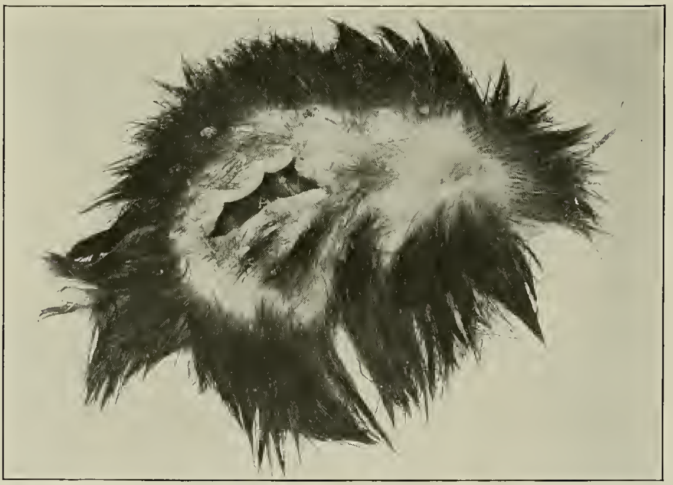

Fig. 60.—Two weeks after direct application of standard droplet to cornea. Specimen obtained by excision of lids and orbital evisceration. Marked depilation, especially at the inner canthus. Characteristic "ruffling" and entropion of upper lid. Corneal cloudiness.

porcelain-like cloudiness. When this involved the entire cornea, as in the case figured, there results a complete opacity of the cornea, so that the iris and pupil can no longer be seen and blindness must be nearly, if not quite, complete. (See Figs. 61, 62, 63, 64, 65.)

THE DOG.—Following the direct application of a standard droplet of liquid dichlorethylsulphide to the cornea of the dog, the changes run closely parallel to those described above for the rabbit and it seems unnecessary to describe them in detail. The earliest changes are identical. At the period, however, at which the rabbit's eye becomes sealed by the adhesion of the lid margins, the powerful orbicularis muscle of the dog prevents this occurrence. As a result there is never the empyema of the conjunctival sac that is found in the rabbit and the exudate seems to be less in amount. The congestion in the earlier stages is more marked, or at least more evident, than in the rabbit. The edema and the corneal necrosis are similar with the exception that the localization of the corneal opacity in the lower segment was never noted.

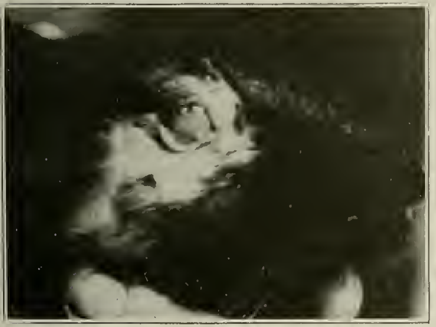

Fig. 61.—Three weeks after direct application of standard droplet to center of cornea. Same rabbit as Fig. 59. Marked ectropion of lower lid. Porcelain-like cloudiness of the cornea most marked in lower half.

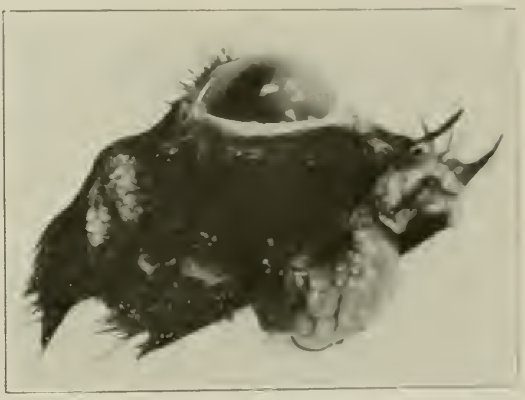

Fig. 62.—Three weeks after direct application of standard droplet of dichlorethylsulphide to cornea. Specimen obtained by excision of lids and exenteration of orbit. Anterior segment of globe [illegible] to show apparent staphyloma of cornea toward the inner canthus. The corneal cloudiness is well shown.

EXPOSURE TO MUSTARD GAS VAPOR

THE RABBIT.—The symptoms and gross pathology produced by exposure to mustard gas vapor vary with the concentration of the vapor and the length of exposure. In any case, they differ in degree, but not in kind, from those produced by the direct application of the liquid dichlorethylsulphide to the cornea and its immediate spread throughout the conjunctival sac by blinking. An exposure for fifteen minutes to a concentration of approximately 1:20,000 was found to give results of about the same degree of severity as those produced by the standard droplet of liquid directly applied. The following notes are abstracted from a protocol of a rabbit subjected to mustard gas vapor for that time and at that strength.

About five minutes after being placed in the gassing chamber the animal commenced to show signs of irritation, increased blinking, rubbing of the eyes and nose, and a change of position to bring the head as far as possible from the affluent opening by which the impregnated air was being introduced. Immediately after removal from the chamber the animal was quiet but after a short interval continued to show increasing signs of irritation of the conjunctival and respiratory mucosa. These continued for the next few hours. At five hours after gassing a well-marked conjunctivitis was present. There was increased lacrimation, redness of the lid borders, beginning edema and a marked photophobia. After sixteen hours the signs and symptoms were all much more marked. The exudate had become somewhat mucopurulent; congestion of the lid borders and conjunctiva was increased and likewise the edema. The animal kept both eyes closed because of the photophobia, which seemed much more marked. The edema reached its height about twenty-four

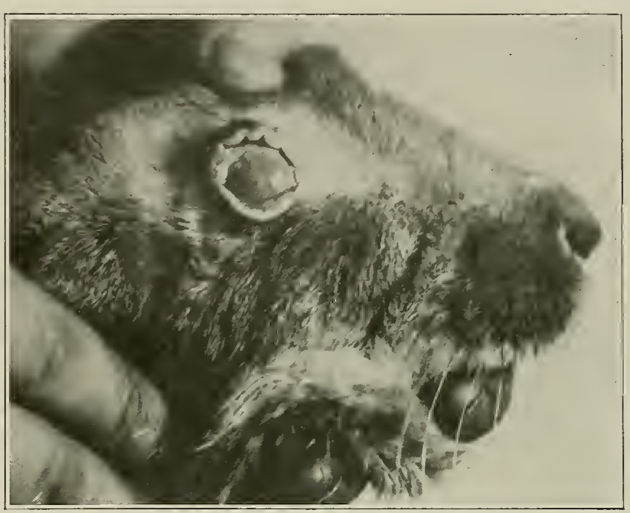

Fig. 63.—Six weeks after direct application of standard droplet to cornea. Combined ectropion and entropion of upper lid with resulting "ruffling" of lid margin. Ectropion of lower lid. Organization of the necrotic cornea with extensive arborizations of newly formed blood vessels, best seen in the upper half of the cornea. Even in the photograph these can be traced from the sclera across the superior arc of the limbus to the central portion of the cornea. The same eye is shown in the next two figures, taken one week later after excision.

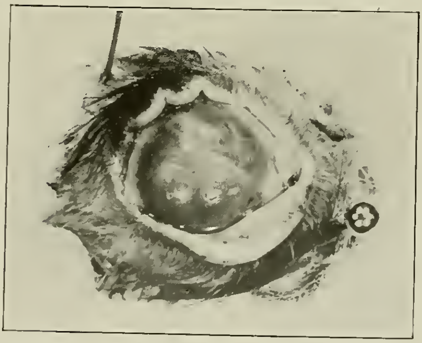

Fig. 64.—Seven weeks after direct application of standard droplet to cornea. Excised specimen. Complete opacity of cornea with vascularization. "Ruffling" of upper lid with areas of entropion and very marked smooth ectropion of lower lid. Apparent irregular staphylomata of cornea are areas of thickening due to infiltration and organization.

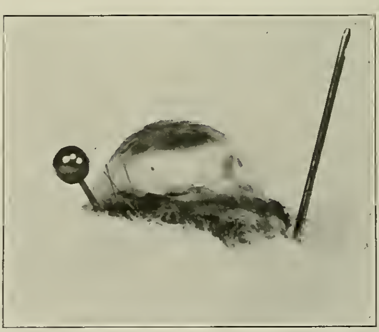

Fig. 65.—Seven weeks after direct application of standard droplet to cornea. Same eye as in preceding figure. Here shown in profile to show marked irregularity of corneal surface. Note especially the prominent apparent staphyloma in the sclera toward the inner canthus.

hours after exposure, and a well marked chemosis was then evident. All skin surfaces where the hair was thin showed a definite erythema. This was especially marked on the lids and convexity of the ears. A bilateral rhinitis with abundant serous exudate also appeared at this time. The inflammatory changes of the upper respiratory tract were much worse at thirty-six hours, the wheezing respiration being distinctly audible at a distance. The eyes were sealed, and upon separation of the lids a large amount of thick purulent exudate appeared. The conjunctivæ were edematous and congested, and there were a few minute subconjunctival hemorrhages.

The lesions progressed slowly as described for those produced by direct application. At seventy-two hours the clouding of the lower half of the cornea had appeared to a marked extent. The lids, having lost their edema to a considerable degree, remained stiff and stood out far from the eyeball, showing the first signs of the "ruffling" previously described. At ninety-six hours the lid borders began to show loss of the necrotic epithelium with the formation of shallow ulcers. The corneal surface became roughened through loss of the epithelium, but no deeper ulceration could be demonstrated.

The lesions produced by this method have not been observed up to the stage of complete healing, as was done with those produced by direct application; but there are no apparent differences in the nature of the sluggish reparative processes in the two cases.

SUBCUTANEOUS INJECTION AND INGESTION OF DICHLORETHYLSULPHIDE IN RELATION TO OCULAR LESIONS

We have attempted to verify the statement of Victor Meyer that subcutaneous injection of dichlorethylsulphide determines the occurrence of a conjunctivitis, indicating not only a metastasis of the toxic substance through the blood stream, but also a selective affinity or special susceptibility of the conjunctiva. For this purpose we have used a series of four albino rabbits, two hares and two dogs. The albino rabbits offered the greatest prospect of success, since in them the slightest conjunctival congestion can be readily seen. In the case of the rabbits and hares one minim of dichlorethylsulphide was given as a subcutaneous injection. In no instance was any trace of conjunctivitis or any other ocular change produced. The site of injection developed a wafer-like induration which dried down to a deep-seated eschar. In every case there developed a foul diarrhea to which most of the animals succumbed on about the sixth day. One large dog received four minims subcutaneously. There was no conjunctivitis, but a severe diarrhea developed, and death occurred on the fourth day. Another dog was fed four minims in meat. Severe burns of the mouth and upper alimentary tract were produced but there was no conjunctivitis. These lesions in the gastrointestinal tract will be considered more fully in a subsequent chapter. Attempts to produce conjunctivitis or other eye lesions by intravenous injection have also failed; although this fact has little weight since death occurs too soon to permit the development of marked changes.

RELATIONS OF PANOPHTHALMITIS TO DICHLORETHYLSULPHIDE LESIONS

In the ocular lesions produced by the standard droplet and by exposure to a vapor concentration of 1:20,000 for fifteen minutes, with ordinary care given to the eyes so treated, by separation of the lids to allow the purulent exudate to drain out, no evidence of panophthalmitis was observed; and by the end of the fourth week healing was usually complete. But in animals exposed as above, with eyes untreated, lids allowed to remain sealed and exudate to accumulate, within three weeks there may develop a purulent panophthalmitis which by the sixth week usually destroys the entire eyeball with complete suppuration of all orbital tissues. When a larger dosage is given, and the eyes untreated, a panophthalmitis may develop more rapidly. (See Fig. 96.)

Protocol.—One series of four rabbits was treated with a heavy application of liquid dichlorethylsulphide to the center of the cornea. The amount applied was about twice that of the standard application. In three rabbits the eyes were left untouched for five weeks, in the fourth for six weeks. After the first sealing of the lids there was no separation of the same to allow the purulent exudate to escape. As a result an empyema of the conjunctival sac developed with subsequent destruction of the eye from a suppurative panophthalmitis. These eyes all showed the same gross picture; perforation of the cornea, necrosis and abscess formation, loss of the contents of the globe, and suppuration of all orbital contents.

In our cases the occurrence of panophthalmitis is due entirely to secondary infection, which occurs ultimately after several weeks in the untreated cases after slight gassing; but much more rapidly after heavier dosage. The pathologic changes produced by dichlorethylsulphide are covered up by those due to secondary infection.

Fluorescein Test

The standard method of applying an alkaline aqueous solution of fluorescein for the determination of corneal ulceration was carried out on a series of eyes at different time intervals following exposures to dichlorethylsulphide. A 2 per cent alkaline watery solution was used. Ten minutes after the direct application of the standard droplet to the center of the cornea, several minute pinpoint areas at the vertex of the cornea retained the fluorescent green coloration. These minute areas increased in number so that, within fifteen minutes after the exposure, the vertex of the cornea appeared peppered with these spots in a small circular area. These pinpoint areas increased in size, and became confluent in about thirty minutes after exposure. By one hour they were fairly uniformly confluent. From this time on the fluorescein staining showed a gradually increasing depth of penetration and a spreading of the circumference of the staining area over the cornea, especially toward the inner canthus. The depth of the intravital staining reaction is greatest at the vertex of the cornea and decreases laterally. At the end of forty-eight hours a narrow crescentic area toward the outer canthus remains unstained showing that the necrosis in this area occurs more slowly than elsewhere. After exposure to the vapor of dichlorethylsulphide the fluorescein staining reactions are the same as after direct application. This intravital fluorescein staining is parallel in intensity to the necrosis of the corneal epithelium as shown by the microscopic study of the same stages. The earliest intravital staining occurs at the same time that the pyknosis of the corneal epithelium becomes evident, before any ulceration or abrasion takes place. The use of this test is therefore of the greatest importance clinically in determining the severity and progress of the lesions and the effects of therapy.

SUMMARY OF GROSS PATHOLOGIC CHANGES

1. The standard drop of 0.0004 c.c. when applied directly to the cornea of animals was found to produce results practically identical with those produced by an exposure of 15 minutes to a vapor concentration of 1:20,000. The criticism, therefore, that the use of the standard drop produces changes not comparable to those observed in exposure to dichlorethylsulphide vapor does not hold. Further, the use of the standard drop is a much more convenient and accurate way, as well as a safer method, of handling this material for experimental purposes. Moreover, the use of the direct application method avoids the complication of respiratory or general cutaneous involvement following the exposure of the animal in a gas chamber.

2. Dichlorethylsulphide produces after one or two minutes exposure to drop or highly concentrated vapor a definite irritation of the conjunctiva with increase of lacrimation. Usually within thirty minutes there is a well-marked hyperemia, followed in an hour by the development of edema, which progresses rapidly up to the twelfth hour when there is usually a well-marked chemosis. Minute subconjunctival hemorrhages may develop as early as the tenth hour.

3. In animals the edema develops first and most markedly in the palpebral conjunctiva, following the direct application, while in the exposure to mustard gas vapor it frequently develops first in the bulbar conjunctiva, this being practically the only difference observed in the effects of the two methods. By the end of the third day the edema begins to subside slightly, but persists to some degree for several weeks. In man the edema is less marked, more irregular, while the hyperemia is more marked, and minute vesicles may be found on the conjunctival surface.

4. The necrosis of the cornea is shown by a definite cloudiness developing in five to six hours which usually at eight hours has reached such a degree that the cornea takes on a porcelain-like appearance in the form of a very characteristic bluish white opalescence. In the mildest cases the lesion does not progress beyond a slight cloudiness. Intravital staining with an alkaline aqueous solution of fluorescein shows very early the development of the corneal necrosis, even before ulceration has occurred. A striking phenomenon is the frequent occurrence of a more opaque band or line running horizontally across the cornea just below its transverse diameter.

5. A seropurulent exudate is well developed by the fifth to the sixth hour and increases until the eyelids are usually sealed by the accumulated exudate by the tenth hour. This adhesion of the lids remains a constant feature until the gradual subsidence of the inflammatory process about the third week. The edges of the lids remain sealed unless forcibly separated. If the eyes are frequently examined with consequent separation of the lids and removal of the accumulated exudate, the stage of purulent exudation is perceptibly shortened.

6. With the subsidence of the edema a characteristic kinking or "ruffling" of the upper lid, a combined entropion and ectropion, appears, usually

by the fifth or sixth day. At the same time the lower lid begins to exhibit a smooth ectropion.

7. Depilation of the lid hairs and of the face hairs, eventually about the entire orbit, takes place.

8. During the second week changes in the corneal curvature are constantly noted, some of these so marked as to appear staphyloma-like.

9. Hypopyon sometimes occurs. Clouding of the contents of the anterior chamber occurs quite regularly in the later stages.

10. From the third week on the lesions slowly progress in a manner characteristic of the mustard gas lesion of the skin towards resolution and repair. The "ruffling" of the upper lid increases up to the eighth week while the ectropion of the lower lid frequently reaches the point of complete eversion. Progressive vascularization of the cornea takes place, the vessels usually reaching the center of the vertex by the end of the sixth week. Corneal cicatrization, marked impairment of vision, and thickening of the eyelids and nictitating membrane are the ultimate sequelæ. Even in the lighter cases in man, the edema and hyperemia of the conjunctivæ tend to run a chronic course with resulting visual disturbances and reduction of vision. An increased susceptibility to the vapor may develop. This susceptibility, however, is not a specific one.

11. Secondary infection. In animals exposed to the standard drop or vapor concentrations of 1:20,000, followed by treatment of the eyes, purulent panophthalmitis has not been observed to develop. In the case, however, of untreated eyes, and following heavier dosage, suppurative panophthalmitis does develop with complete destruction of the eyeball.

II. Microscopic Pathology

TECHNIC.—Every care was taken to prevent the formation of artefacts, either postmortem or technical. The eye was removed at once from the freshly killed animal by a wide incision encircling the lids and eviscerating the orbit. It was at once placed in the fixing fluids, a neutral formol being used for the greater part. The specimen was left in the fixing fluid about forty-eight hours before being sectioned, at which time uniform blocks of tissue were selected. These were so oriented as to give vertical sections through the entire eyeball, a section through the inner canthus and one through the lacrimal gland from each eye. The lens was removed from the eyeball after thorough hardening, in order to facilitate the cutting of thin sections. These tissues were embedded in paraffin, the sections were transferred to the celloidin sheet and stained with hemalum and eosin and by other ordinary staining methods.

RABBIT.—*One-quarter Hour.*—The changes observed are of slight degree, consisting of contraction and pyknosis of the corneal epithelium which is more marked at the vertex and less marked over the limbus. Likewise the cells of the substantia propria show a slightly greater degree of pyknosis and contraction than in control preparations. The bulbar and palpebral conjunctivæ show a similar pyknosis and contraction. In the fornix there is a more decided vacuolation of the conjunctival epithelium. The epithelium of the cutaneous surface of the eyelid shows also slight pyknosis and contraction. In the region of the inferior fornix alone does the subconjunctival connective tissue show a well-marked edema. In the upper fornix the edema is less marked. The lacrimal gland shows a marked distention of its gland spaces which are filled with secretion. Harder's gland and the tarsal glands show no changes, likewise the sinus hairs. The blood vessels of all parts are anemic rather than congested. There is no hemorrhage and no thrombosis.

One-half Hour.—Changes identical with those above, except a little more marked in degree. Pyknosis and vacuolation are a little more pronounced. The edema is much greater, particularly around the lacrimal gland. The distention of the lacrimal gland is greater, and its cells show a marked vacuolation. Greater congestion in all parts.

One Hour.—The only changes are an increase in the edema and congestion.

One and One-half Hours.—The pyknosis of the corneal epithelium is as above, but the substantia propria shows a distinctly more marked pyknosis of the corneal cells extending entirely through the cornea at the vertex. A large portion of the endothelium of the anterior chamber shows marked pyknosis and contraction. The conjunctival epithelium, both bulbar and palpebral, shows an increased degree of pyknosis while the subconjunctival connective tissue shows now a marked edema, extending entirely through the eyelids. It is especially noteworthy that many of the blood vessels appear partly collapsed, with a relative anemia, while others are moderately congested. The lacrimal gland shows the same active secretion, many of the acini being greatly dilated, and filled with secretion. The vessels of the gland are congested and there is an increased number of wandering cells throughout the gland. The stroma of the gland and the surrounding tissues show extreme edema. The tarsal glands show groups of pyknotic alveoli. The epithelium of the membrana nictitans shows less change than that of the bulbar and palpebral conjunctivæ.

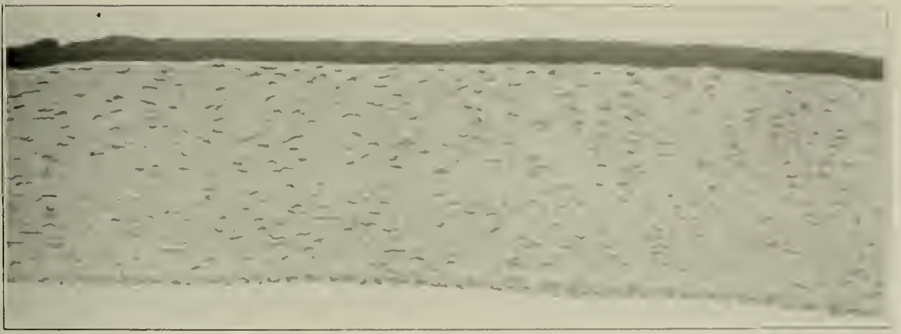

Fig. 66.—Cornea two hours after application of standard droplet. First stage of necrosis of corneal epithelium and of the cells of the interstitial substance. Marked pyknosis of the corneal epithelium, the cells of the lowest layer alone being barely distinguishable. The nuclei of the interstitial substance and of the endothelial lining of the anterior chamber are also pyknotic. Section taken at corneal vertex.

Two Hours.—(See Fig. 66.) Pyknosis of the corneal epithelium is complete. It is impossible to recognize the individual cells. The substantia propria stains more diffusely blue and the endothelium of the anterior chamber shows a greater degree of pyknosis and vacuolation. Similar changes occur in the palpebral and bulbar conjunctivæ and in the epidermis of the eyelids. The edema of the eyelids is now extreme, being most marked on the conjunctival surface. (See Fig. 80.) There is an increase of wandering cells throughout both upper and lower eyelids, but no well-marked cellular infiltrations. Many of the blood vessels show a well-marked congestion. The membrana nictitans shows a marked pyknosis of its epithelium and a marked edema of its stroma, its thickness being increased about tenfold. The lacrimal gland shows a marked distention of all its gland spaces and a marked vacuolation of its epithelium which appears distinctly more columnar in shape. The cells of Harder's gland stain very deeply and are contracted and pyknotic and have lost their granular appearance to a marked degree. The Meibomian glands show a similar marked pyknosis involving all of the alveoli. The adipose tissue around the eye and about the tarsal glands shows a marked edema and gives a marked mucin staining reaction.

Three Hours.—The cornea is as before. The epithelium of the conjunctiva, both bulbar and palpebral, shows a greater degree of necrosis. The edema is much more marked beneath both the bulbar and palpebral conjunctiva, amounting almost to a liquefaction of the tissue. There is now a well-marked polynuclear infiltration beneath the conjunctival epithelium and extending throughout the entire lid. The epidermal surface of the eyelids shows now a well-marked pyknosis and karyorrhexis of the nuclei of the dermis, particularly of the papillary layer, with a well-marked polynuclear infiltration, the changes being identical with those described in the chapter on the skin lesions, with the exception that the cellular infiltration is somewhat more prominent than was found in the skin. The vessels show a more marked congestion than in any of the previous stages. The lacrimal gland shows the same distention of the alveoli but the cells are less columnar and the nuclei show some pyknosis and karyorrhexis. The gland of Harder and the tarsal glands show the same pyknosis as in the preceding stage. The changes in the epidermal surface of the eyelid have advanced in necrosis and cellular infiltration.

Four Hours.—Changes in the cornea appear as in the preceding. Bulbar and palpebral conjunctivæ, membrana nictitans and epidermal surface of eyelids show increasing edema and cellular infiltration. The lacrimal gland shows extreme distention and the cells of many acini are flattened and vacuolated as in a state of exhaustion atrophy. Harder's gland presents a well-marked vacuolation of its epithelium, many of the cells showing large clear droplets, edema. Likewise the tarsal glands show edema. In the palpebral and bulbar conjunctivæ the cellular infiltration is increased, and the lymph follicles in the palpebral conjunctiva contain great numbers of wandering cells. Vessels are greatly congested.

Five Hours.—(See Fig. 67.) The corneal epithelium is in part desquamated over the region of the vertex, and about this the epithelium shows marked dissociation and vacuolation. The substantia propria now stains lighter in color, many of its nuclei being only shadows. At the sclerocorneal junction there is now a well-marked infiltration of polynuclears, most marked just beneath the pyknotic epithelium. The upper and lower lids show extreme edema (see Fig. 81); and there is a marked infiltration of polynuclears throughout, which is more marked beneath the palpebral conjunctiva near the palpebral border. In this region the conjunctival epithelium is desquamating and there is developing an ulcerating surface. The adherent dead epithelium is infiltrated with polynuclears. The blood vessels show congestion. There is no thrombosis. On the epidermal border of the lids there is beginning desquamation of the dead epidermis. The sebaceous glands near the margin of the lid show sebum retention. Likewise on the lower lid near the palpebral margin, there is noted the first development of ulcer or slough, and the membrana nictitans shows loss of its epithelium in areas. Lacrimal, Harder's and tarsal glands, as in the preceding.

Six Hours.—Changes identical with above.

Eight Hours.—The only change noted from above is an increase in the extent of the ulcer on the conjunctival surface near the palpebral margin in both upper and lower lids, more marked in the upper. (See Fig. 82.)

Ten Hours.—Cornea shows gradual loss of chromatin. Stains more palely.

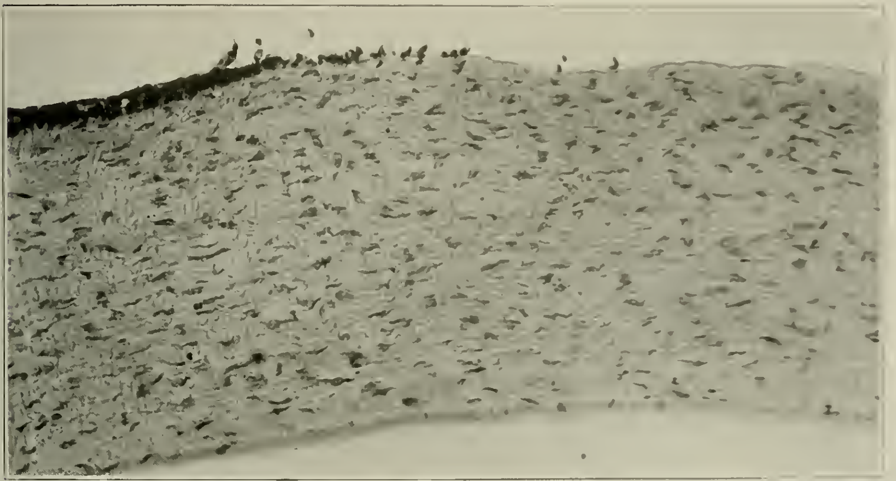

Fig. 67.—Section of cornea at vertex five hours after direct application of standard droplet. Desquamation of necrotic epithelium in center of vertex. Pyknosis of remaining epithelium and of cells of the interstitial substance. Complete necrosis of endothelial cells of anterior chamber.

On the eyelids the necrosis of the epidermis and eschar formation have progressed while almost the entire conjunctival epithelium is completely disintegrated, forming a granular layer infiltrated with polynuclears. The exudate is most marked near the palpebral border where there is a distinct ulcer covered with exudate. Intense edema and congestion as in the preceding. Small pinpoint hemorrhages occur in the subconjunctival connective tissue. Both the lacrimal and Harder's glands show more marked vacuolation. Increased polynuclear infiltration throughout, extending even into the orbital tissues.

Twelve Hours.—At the corneal vertex the cornea is dead throughout having completely lost its nuclei. The corneal epithelium is desquamated over the vertex, and only here and there are there faint outlines of the nuclei of the substantia propria. The pyknotic and vacuolated endothelium of the anterior chamber is still intact. The escharization of the epidermal surface of the lids is complete, and desquamation of both bulbar and palpebral conjunctival epithelium is nearly complete. Congestion is very marked and there are numerous minute hemorrhages by diapedesis both beneath the epidermal surface and in the subconjunctival connective tissue. The edema is even more marked than in the preceding stages, involving the whole eyelid, and the lymphatics are enormously distended. The lacrimal gland is as before, but Harder's and the tarsal glands show marked edema and liquefaction necrosis. There are masses of exudate, rich in polynuclears, adherent to the conjunctiva at the lid margins, the result of drying and concentration of the secretion, but near this, minute collections of polynuclears beneath the conjunctiva suggest beginning infection. The fluid of the edema now assumes the same hyaline, finely granular, deeply pink staining appearance as found in the subcutaneous tissues. (See Chapter on Skin Lesions.)

Fourteen Hours.—Changes as above, but slightly advanced. Intense congestion. Polynuclear infiltration of the muscle. Numerous hemorrhages about the greatly distended vessels. Secondary thrombosis beginning. More marked polynuclear infiltration into the subconjunctival connective tissue. Heavy granular precipitate in the distended alveoli of the lacrimal gland. These contain, likewise, great numbers of albuminous spherules, staining deep violet or pink, derived from the disintegration of the cells.

Fifteen Hours.—Changes as above with more marked polynuclear infiltration at the sclerocorneal junction, in the ocular muscles and in the orbital tissues. Beginning infection of the conjunctival ulcers near the palpebral border. Diffuse inflammation of the entire peribulbar tissues. It is a notable fact that the sebaceous glands on the epidermal surface of the lids show penetration with the dichlorethylsulphide and necrosis, while the large ones at the palpebral margin seem to escape.

Sixteen Hours.—Complete loss of the necrotic epithelium over the corneal vertex. Increasing polynuclear infiltration at the sclerocorneal junction. Edema of the ciliary body and ciliary ring. Increasing polynuclear infiltration and greater collection of pus at the palpebral borders.

Eighteen Hours.—Nearly complete necrosis of the cornea, except toward the periphery of the limbus. On the lids escharization is extending, the necrosis reaching into the subconjunctival tissue and into the subepidermal tissues on the cutaneous side. It is notable, however, that the subcutaneous necrosis is deeper than the subconjunctival. On the skin surface the necrosis extends nearly through the depth of the lower border of the sebaceous glands. The epithelium of the entire margin of the lids is now completely necrosed and desquamated. Over the entire surface of the conjunctiva including the membrana nictitans the epithelium is now necrotic and desquamating, but the necrosis extends but very little into the subepithelial connective tissues. For the first time changes are observed in the erectile sinus hairs of the upper lid, the epithelium of the hair follicle showing some pyknosis and contraction.

Twenty Hours.—Complete necrosis of the cornea, in the central portion extending to the endothelial lining of the anterior chamber which is partly necrotic and desquamating. Conjunctival, lid and gland changes as above. The large sebaceous glands at the lid margin show a more marked polynuclear infiltration than in any of the preceding. Congestion, edema and minute hemorrhages as in preceding stages.

Twenty-two Hours.—Complete death of cornea in central portion, with loss of epithelium and endothelium of anterior chamber. Only scattered nuclei through the dead substantia propria. Eyelids show the same extreme edema, congestion and numerous hemorrhages by diapedesis around the congested vessels as in the preceding, but with an increasing small-celled infiltration. Fibroblastic proliferation first observed in the subconjunctival connective tissue.

Twenty-four Hours.—Cornea completely necrotic except near the sclerocorneal junction. Its laminæ are separated and there is a collection of fluid between the separated laminæ. Edema at its height; other changes as above.

Twenty-six Hours.—Necrosis of the cornea complete with marked separation of the laminæ into irregular spaces. Edema as in preceding, but polynuclear infiltration much more marked extending throughout the entire thickness of the lids. Marked distention of the acini and atrophy of the cells of the lacrimal gland. Numerous capillary hemorrhages by diapedesis throughout the subconjunctival tissues, and the dermis of the lids. (See Fig. 84.)

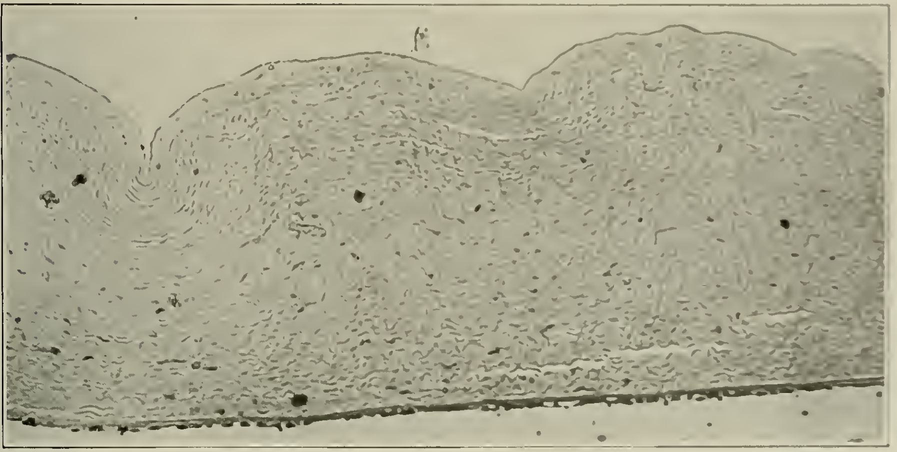

Fig. 68.—Cornea thirty hours after exposure to vapor of dichlorethylsulphide. Complete necrosis of cornea

Twenty-eight Hours.—As in the preceding, no difference.

Thirty Hours.—(See Fig. 68.) Identical with the preceding stages.

Thirty-two Hours.—Most marked changes in the cornea, particularly at the vertex. Surface roughened, knobby, laminæ separated. Changes in lids and glands as in preceding.

Thirty-four Hours.—The central portion of the cornea shows complete necrosis but at the periphery there is a marked cellular infiltration and proliferation of corneal cells. At the sclerocorneal junction there is an evident fibroblastic proliferation. The edema of the upper palpebral conjunctiva is less marked; cellular infiltration about as before, but more cells of a fibroblastic type. The edema of the lower lid is the most marked yet seen, a large portion of the subconjunctival connective tissue showing complete liquefaction necrosis with marked polynuclear infiltration. (See Figs. 85, 86.) The cutaneous border of the lower lid shows a marked depilation, almost every hair having been shed. The upper lid shows a less marked depilation. The lacrimal gland shows in various areas a very marked hypertrophy of the cells. These are more columnar with a very deeply staining protoplasm. Other portions show the light vacuolated cells as described above.

Thirty-six Hours.—Changes as in the preceding, except for the membrana nictitans which shows marked congestion of its vessels and multiple capillary hemorrhages. The ocular muscles show marked edema.

Thirty-eight Hours.—The most marked necrosis of the cornea, the complete necrosis extending almost to the sclerocorneal junction. Complete necrosis of the endothelial lining of the anterior chamber with increased number of leucocytes in the fluid of the anterior chamber. On the lids there is beginning regeneration of the epidermis and hair follicles, but no evidences of regeneration of the conjunctiva. Almost complete depilation. Edema persistent in the subconjunctival tissues, and at the palpebral margins there is a marked collection of pus.

Forty Hours.—Necrosis of cornea less marked than in preceding individual; endothelial lining preserved. Appearances indicate a somewhat earlier stage, probably due to less intense action.

Forty-two Hours.—(See Fig. 69.) Marked necrosis of the central portion of the cornea. The membrane of Descemet and the endothelium of the anterior chamber appear as a hyaline red line bordering the anterior chamber. Proliferation of corneal cells at border of cornea; fibroblastic proliferation at sclerocorneal junction. Beginning separation of eschar on epidermal side of lids and also on the conjunctiva. Cutaneous lesion much deeper and more severe than the conjunctival, although the edema is much more marked on the conjunctival side, as is also the leucocytic infiltration.

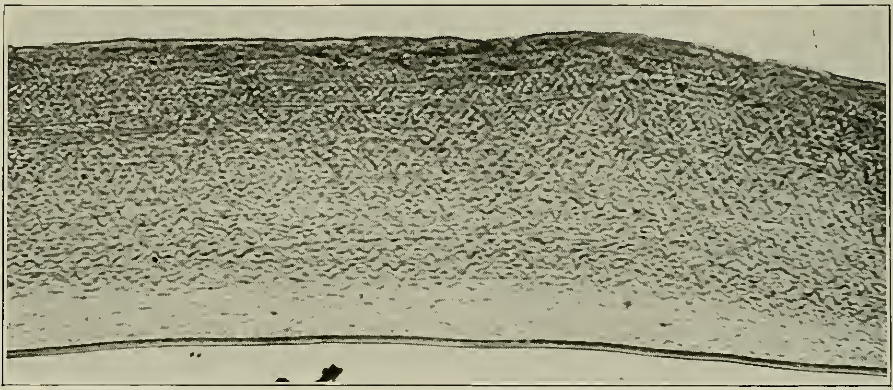

Fig. 69.—Cornea forty-two hours after application of standard droplet. Membrane of Descemet appears as a bright hyaline line staining red with eosin.

Forty-four Hours.—Changes the same as at forty-two hours but of less intensity. Probably due to dilution of dose on the cornea. The skin surface of the lids shows marked escharization.

Forty-six Hours.—No essential differences.

Forty-eight Hours.—Corneal changes same as in the preceding. More marked escharization of the lids and conjunctival surfaces. Beginning separation of the eschar on epidermal portion of lids. Almost complete depilation.

Fifty Hours.—Very marked separation of corneal lamellæ and formation of irregular spaces. Partial separation of the slough on the cutaneous surface of the eyelids. Well-marked regeneration of the hair follicles. Old hairs nearly entirely shed. The membrana nictitans is markedly hemorrhagic. The large sinus hairs show marked necrosis of the epithelium of the hair follicle. Very marked fibroblastic proliferation in upper lid.

Fifty-four Hours.—Changes as in preceding, except for more marked escharization of the epidermal surface of lids, and more marked fibroblastic proliferation of the subcutaneous tissue. Marked congestion and numerous hemorrhages, particularly on the epidermal side of the lids.

Sixty Hours.—Shrinking and drying of the cornea at its vertex. Fibroblastic proliferation on the dermal side of the lids very marked. Epithelial regeneration well advanced. Beginning regeneration of conjunctival epithelium, but the greater part of the conjunctiva remains denuded. The lower lid shows many hemorrhages throughout its substance; the hemorrhages are more marked than in any other case. The eschar on the dermal side has completely separated with regeneration of the epidermis and hair follicles. Very few of the old hairs are left. Edema is still persistent on the conjunctival side. but less marked.

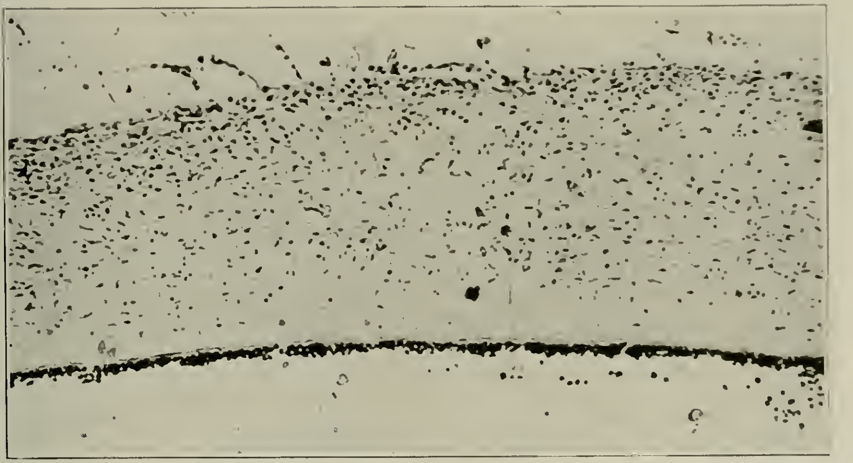

Fig. 70.—Cornea three and one-half days after application of standard droplet. Complete necrosis of corneal tissue; ulceration of surface; beginning infiltration with polynuclear leucocytes and collection of polynuclear leucocytes along the line of the necrotic endothelium.

Sixty-five Hours.—Cornea shows regeneration of the corneal cells throughout its entire extent, but most marked at the periphery. There is marked regeneration of the endothelium of the anterior chamber with plasmodial masses of epithelium on the surface. Anterior chamber contains large numbers of leucocytes. Lids show marked edema, extreme congestion and multiple hemorrhages. Eschar on epidermal side is very deep and not completely separated. Changes much more severe than in the preceding instance with less regeneration and repair.

Seventy-two Hours.—Edema of lids still very marked. Deep escharization on epidermal side with eschar separating. Very little regeneration and repair. In the lower lid the edema is very marked, with liquefaction necrosis of the subconjunctival connective tissues.

Eighty-four Hours.—(See Figs. 70, 71.) Complete necrosis of cornea with no evidence of repair except at the limbus. Very marked congestion and numerous hemorrhages in the lids. Nearly complete depilation with regeneration of epidermis and hair follicles. Membrana nictitans markedly hemorrhagic and shows some fibroblastic proliferation.

Ninety-six Hours.—Cornea completely necrosed in the vertex. Proliferation of corneal cells toward the limbus. Fibroblastic proliferation near sclerocorneal junction. Very deep escharization of epidermal side of lids with separation of eschar. (See Figs. 87, 88.) Regeneration of conjunctival epithelium in various portions of both upper and lower lids. Edema of lids much less marked, but lids are thickened by the marked fibroblastic proliferation.

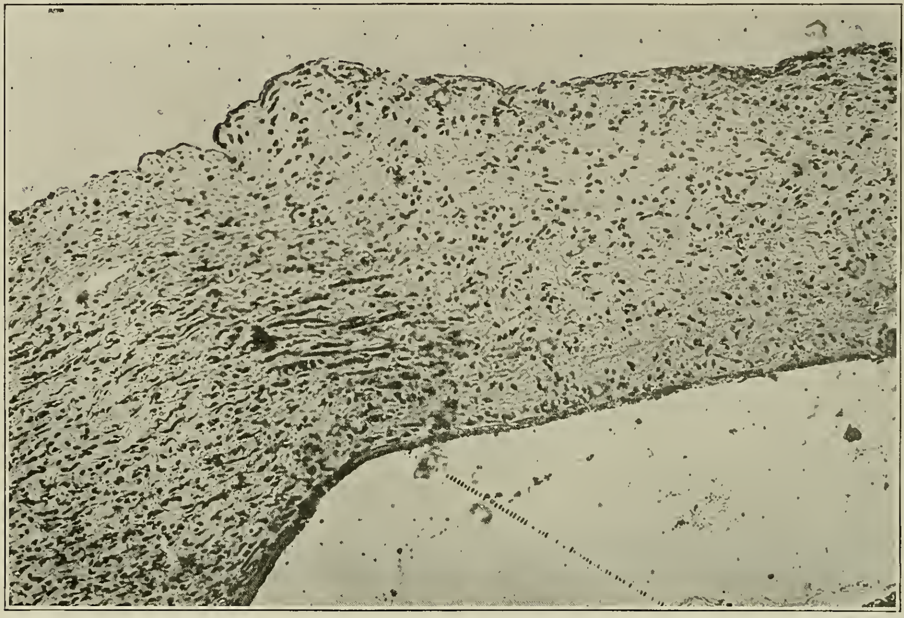

Fig. 71.—Section of sclerocorneal junction, three and one-half days after application of standard droplet. Infiltration of leucocytes, beginning fibroblastic and angioblastic proliferation.

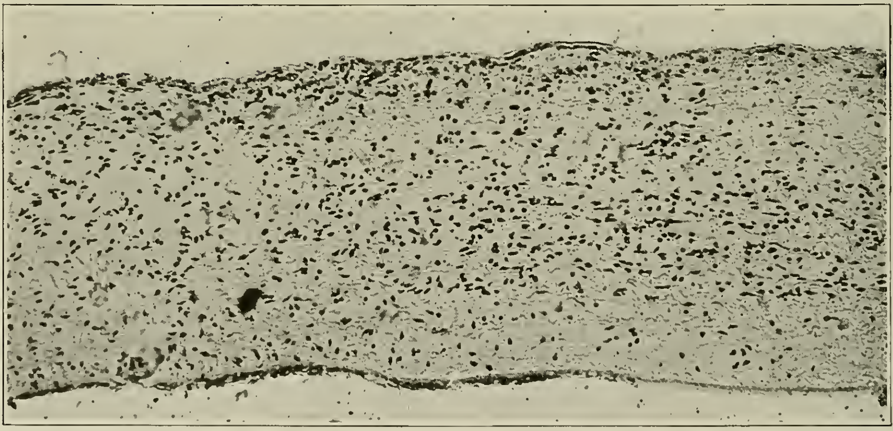

Fig. 72.—Section of corneal vertex seven days after application of standard droplet. Ulcerated surface. Infiltration of necrotic cornea with polynuclears and scattered fibroblasts. Beginning regeneration of endothelium.

One Hundred Ten Hours.—Cornea completely necrosed in central portion. At limbus it shows polynuclear infiltration and fibroblastic proliferation. Anterior chamber contains numerous polynuclears, pus. Iris and ciliary body show cellular infiltration. Conjunctiva shows areas of regeneration of epithelium. Edema is less marked. The gland of Harder shows liquefaction necrosis, as do also the tarsal glands. Necrosis of the epidermal side is deep, but the eschar has nearly completely separated and there is regeneration of the epithelium in some areas and of the hair follicles. Edema of lids is much less marked but the lids are thickened by the connective tissue proliferation. The membrana nictitans shows almost complete regeneration of its epithelium.

Five Days.—There is some regeneration of the corneal epithelium and proliferation of corneal cells and infiltration of leucocytes throughout the entire cornea. The edema of the bulbar conjunctiva is still very marked while that of the palpebral is very much less. The subconjunctival lymph follicles are very hyperplastic. Large dilated lymphatics show, however, in the subconjunctival connective tissue of the lids. The escharization of the epidermal side is very deep extending below the hair follicles, and there is no repair. In the lower lid the edema fluid shows marked fibrin formation.

Six Days.—Regeneration of the corneal epithelium over the limbus and extending in a delicate layer over the vertex. Endothelium of anterior chamber is regenerating. Marked regeneration of the epithelium of the palpebral conjunctiva with overformation of epithelium. Regeneration less marked on the epidermal surface. Lymph follicles hyperplastic. The bulbar conjunctiva still shows marked edema without much cellular infiltration.

Seven Days.—(See Fig. 72.) Marked regeneration of the cornea with great thickening, the cornea being more than twice as thick as normal but the thickness varying in different portions. Marked infiltration of leucocytes and marked proliferation of the cells of the substantia propria. Around the periphery there is a marked formation of new blood vessels extending into the limbus and reaching nearly to the vertex. Marked regeneration of the endothelium of the anterior chamber. Sections cut in some planes of the cornea show a failure of regeneration of the corneal epithelium and a very marked infiltration of the anterior lamellæ. The conjunctival epithelium shows marked regeneration while the eschar of the epidermal portion of the lids has not yet separated. The bulbar conjunctiva still shows marked edema of the subconjunctival tissue. The lids are thickened by the marked fibroblastic proliferation. There is intense congestion and many capillary hemorrhages.

Eleven and One-half Days.—Cornea thickened irregularly from leucocyte infiltration and proliferation of cells of the substantia propria. At the periphery the escharization is quite marked extending onto the bulbar conjunctiva, beneath which there is a marked leucocytic infiltration. The conjunctiva shows marked regeneration of its epithelium, infiltration of the subepithelial tissue and hyperplasia of the lymph nodes. On the epidermal surface there is a very marked eschar formation which is partly adherent and partly separated. Beneath it there is advanced regeneration of the surface epithelium and of the hair follicles. The membrana nictitans is much thickened, its epithelium nearly regenerated, and it shows a marked proliferation of new blood vessels with very hypertrophic endothelium.

Twelve and One-half Days.—Changes identical with the preceding. The hyperplasia of the subconjunctival lymph nodes is very marked.

Two Weeks.—Cornea very irregular in thickness. Shows less evidence of regeneration and repair than the preceding. New blood vessels extending into

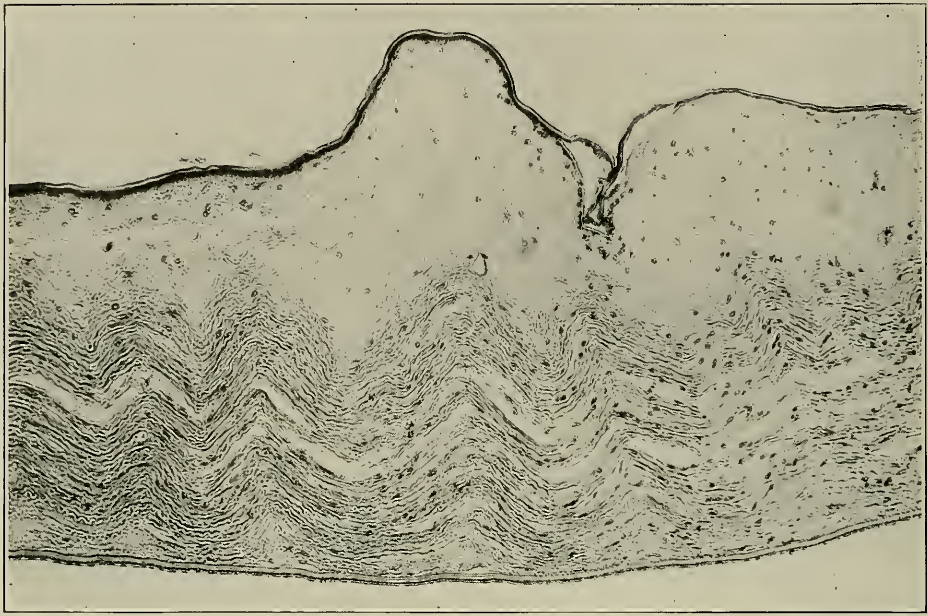

Fig. 73.—Section of corneal vertex four weeks after application of standard droplet, showing the marked irregularities in the corneal surface; regeneration of corneal epithelium and endothelium of anterior chamber; edema of the interstitial substance with some fibroblastic repair.

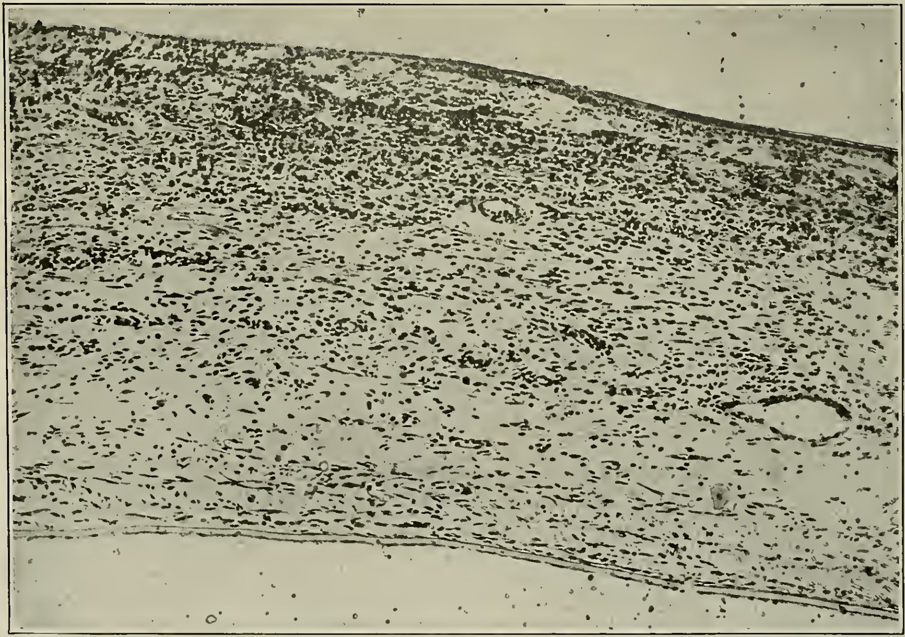

Fig. 74.—Sclerocorneal junction of same eye as in preceding figure, four weeks after application of standard droplet, showing vascularization and repair proceeding from the sclera.

it from the periphery. Eyelids show marked regeneration of epithelium both on the conjunctival and on the skin side. Large nests of cells proceeding from the hair follicles.

Three Weeks.—Regeneration of corneal epithelium and endothelium of anterior chamber. Marked proliferation of blood vessels around the periphery of cornea and formation of scar tissue replacing the corneal substantia propria. Great irregularity in thickness of cornea. Eyelids show advanced repair and regeneration of the epidermal surfaces and of the conjunctival surface. Edema still present on the conjunctival side. The regenerating hair follicles and sebaceous glands form large atypical cell nests. The sinus hairs show fibroblastic obliteration of the cavernous spaces and atypical proliferations of squamous epithelium suggesting newly formed sebaceous glands.

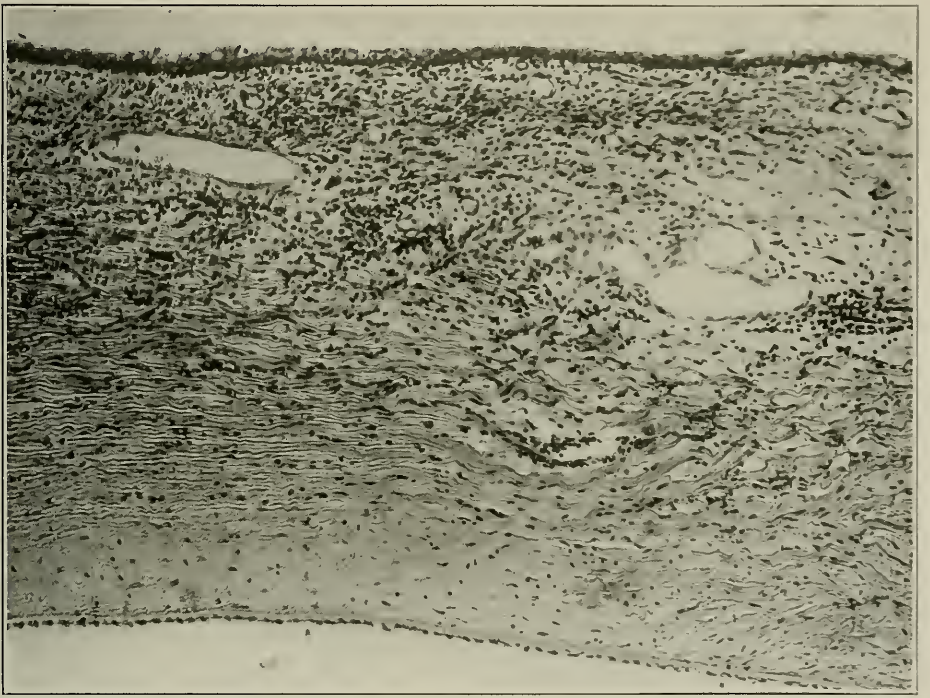

Fig. 75.—Section of corneal limbus four weeks after application of standard droplet. Advancing repair into the cornea from the sclerocorneal junction.

Four Weeks.—(See Figs. 73, 74, 75.) The cornea shows throughout regeneration of its epithelium and of the endothelium of the anterior chamber. It is very irregularly thickened and has an uneven surface. From the periphery great numbers of newly formed vessels extend up toward the corneal vertex, on one side reaching half way across the cornea. These vessels are much more numerous on the anterior side of the cornea and many of them are very large and dilated. On one side near the scleral junction there is a large area of subepithelial edema infiltrated with leucocytes producing an elevation on the cornea as described in the gross notes. Other sections of the cornea show it

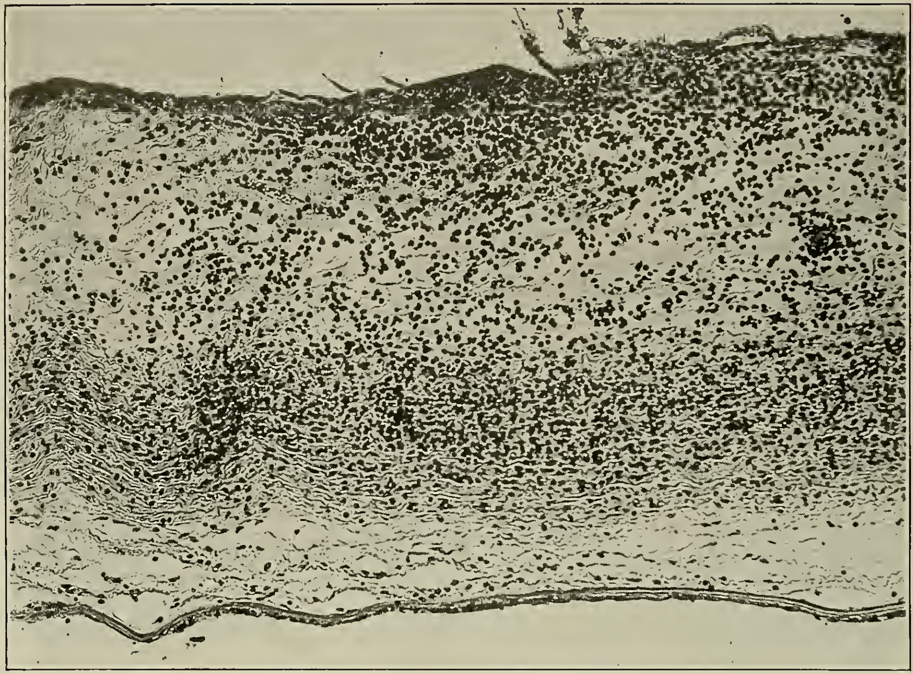

Fig. 76.—Section from the inferior portion of the cornea seven weeks after application of the standard droplet. Persistent ulcer; marked polynuclear infiltration of the cornea and repair. Blood vessels have reached the center of the cornea.

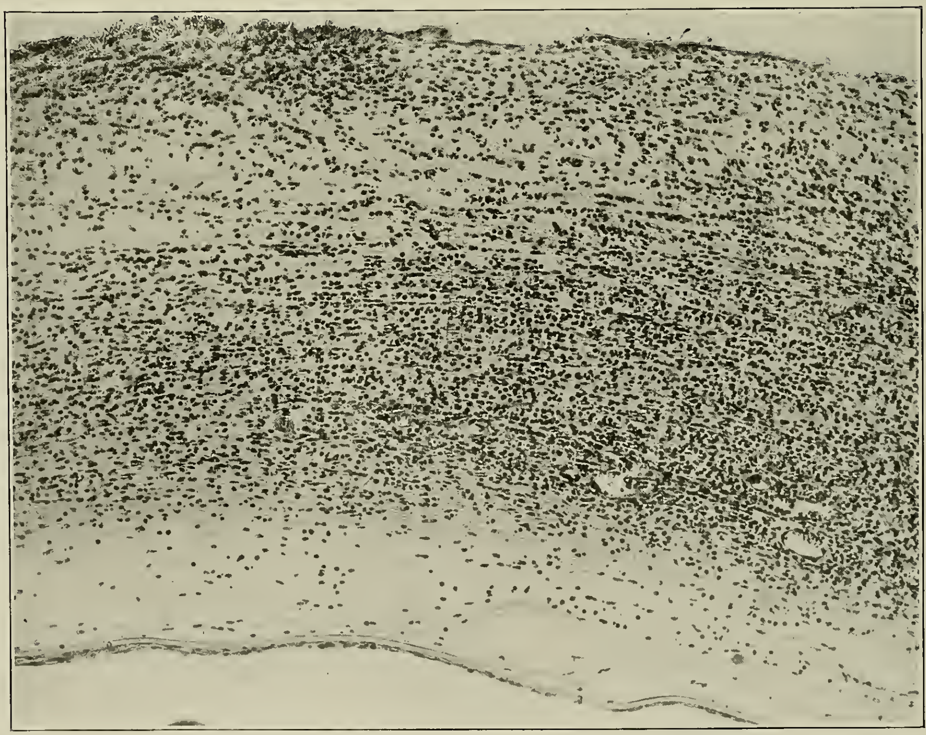

Fig. 77.—Section from inferior portion of corneal limbus, seven weeks after application of standard droplet. Partial regeneration of corneal epithelium. Marked polynuclear infiltration and advanced vascularization and repair of the substantia propria. Regeneration of the endothelium of the anterior chamber.

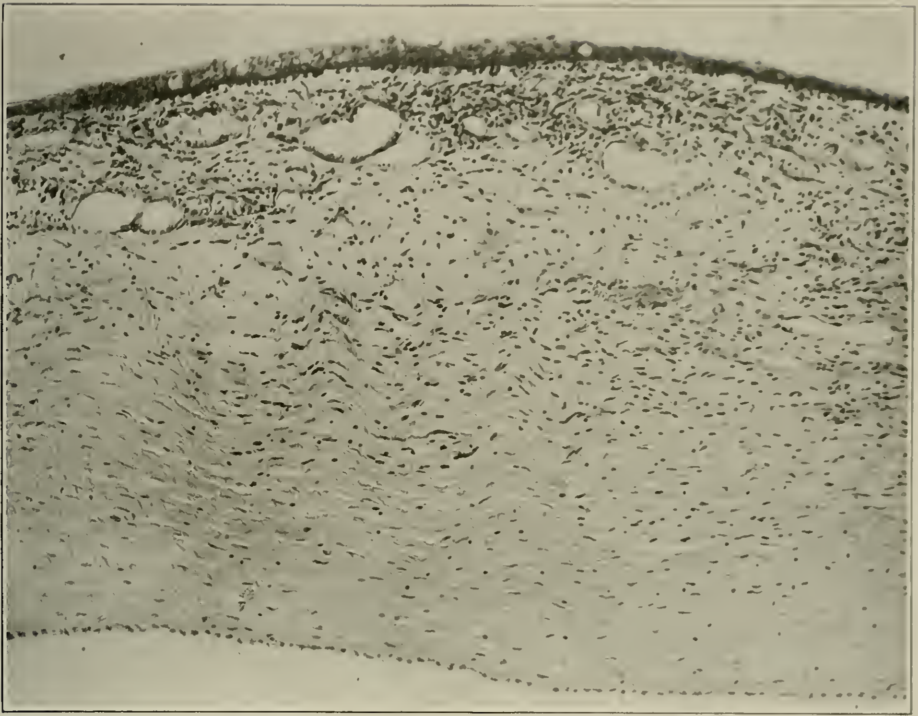

Fig. 78.—Section from the superior half of the corneal vertex seven weeks after application of standard droplet, showing the greater degree of cicatrization usually found in this portion.

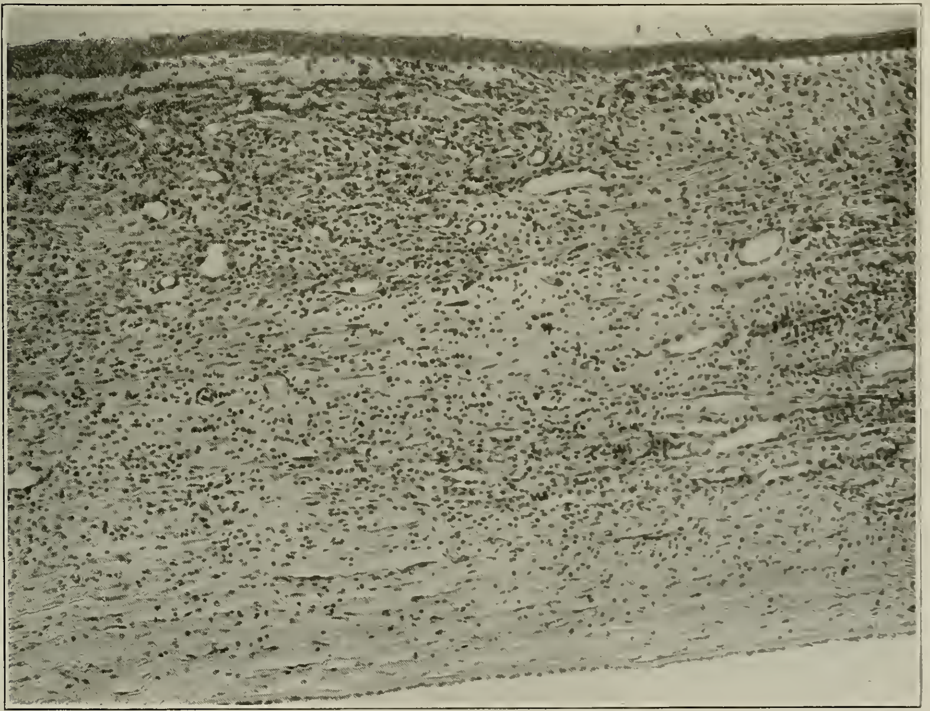

Fig. 79.—Section of corneal limbus from same eye as the preceding figure, showing advanced cicatrization.

to be heavily infiltrated with pus cells between the newly formed blood vessels. Regeneration of conjunctival epithelium is complete except near the palpebral margin where there is still an ulcer. Edema of the subconjunctival tissues is much less marked than in the preceding. Harder's and the tarsal glands show marked lymphoid infiltration. Lacrimal gland more normal in appearance. Hair follicles show new formation of hairs. The large sebaceous glands at the palpebral margin are hyperplastic and the lymph nodes of the conjunctiva are also hyperplastic.

Seven Weeks.—(See Figs. 76, 77, 78, 79.) The cornea is markedly but very irregularly thickened throughout, heavily infiltrated with leucocytes and shows throughout its extent a marked new formation of blood vessels. Substantia propria is largely replaced by fibrous connective tissue. The membrane of Descemet shows as a clear hyaline line and the endothelium of the anterior chamber is regenerated in a flat layer over this. The regeneration of the epidermal surface of the lids is complete; the sebaceous glands are approaching normal size. The edema has almost entirely disappeared except over the bulbar conjunctiva. Lacrimal gland is still hypertrophic. Lymphoid tissue in Harder's gland is hyperplastic, as are also the subconjunctival lymph nodes. The lids and nictitating membrane are thickened from the new formation of connective tissue.

THE DOG.—A smaller series was also carried out upon dogs. The changes are essentially the same in kind, although apparently of greater intensity. A marked hemorrhagic condition of the conjunctiva was noted in the earlier stages.

EXPOSURE TO DICHLORETHYLSULPHIDE VAPOR

THE RABBIT.—Series of animals exposed for varying periods to varying concentrations of mustard gas vapor (1:20,000-1:50,000) and killed at intervals of twelve hours to four days after exposure in the gassing chamber showed changes precisely the same in kind as the animals treated with the standard droplet of the liquid. It was found that a fifteen minute exposure to a 1:20,000 concentration produced changes identical in degree with those produced by the standardized drop of liquid. It is noteworthy in these experiments with the weaker concentrations of the gas that the cornea first showed evidences of necrosis and then the skin surface of the lids, while the conjunctival epithelium did not undergo necrosis, and the conjunctiva itself presented only the picture of a mild conjunctivitis with an unusual degree of edema, particularly of the bulbar conjunctiva in the earlier stages, and of the palpebral in the later. The epidermal changes were in all cases much more severe than the conjunctival, marked necrosis of the former occurring when no necrosis of the conjunctival epithelium was observed. The corneal necrosis was always most severe at the corneal vertex. In all cases exposed to the gas the lesions are most intense in the portion of the conjunctiva and cornea exposed in the palpebral fissure, and the lesions therefore are much less diffuse than when direct application is used, thus resembling more nearly the human cases.

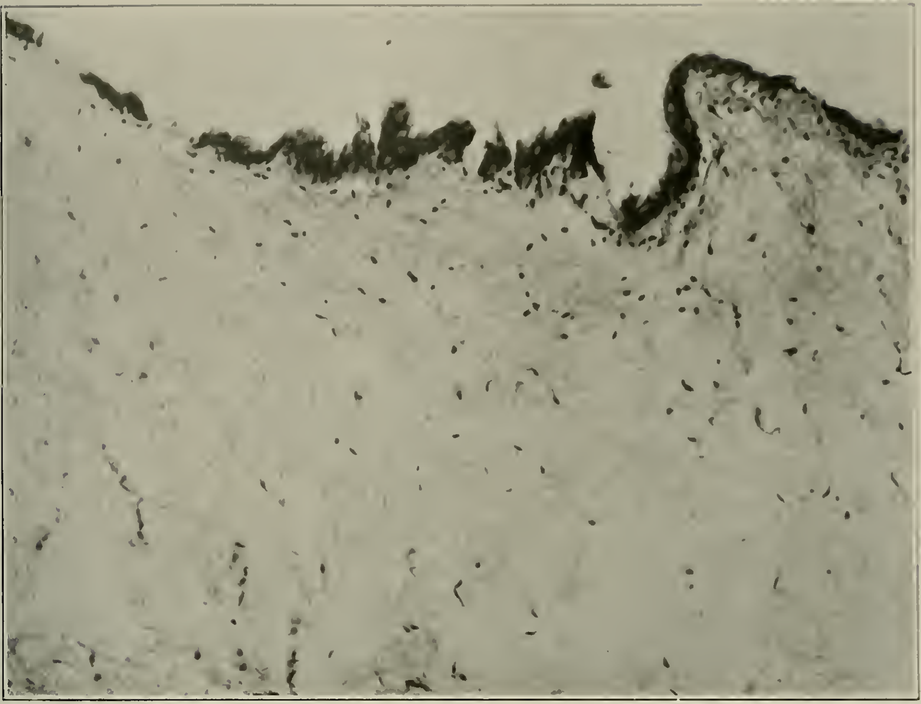

Fig. 80.—Bulbar conjunctiva two hours after application of standard droplet. Pyknosis of conjunctival epithelium and marked edema of the subepithelial connective tissue.

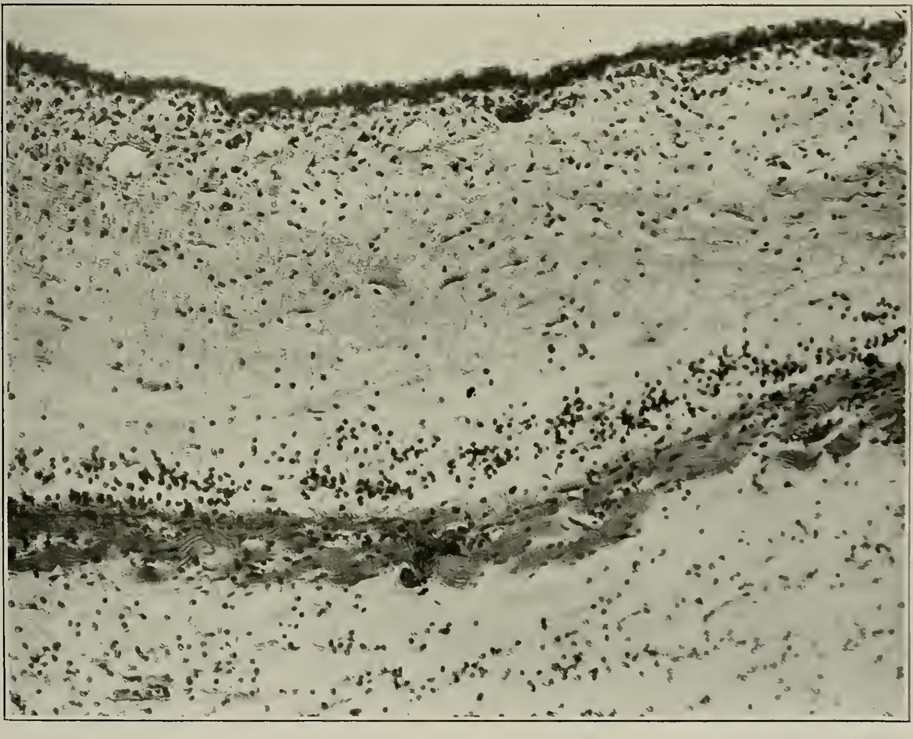

Fig. 81.—Section of palpebral conjunctiva five hours after application of standard droplet. Pyknosis of conjunctival epithelium. Edema of subconjunctival connective tissue. Polynuclear infiltration.

DIRECT APPLICATION OF MUSTARD GAS LIQUID TO THE EYES OF DEAD ANIMALS, THE EYES SO TREATED BEING EXAMINED AT INTERVALS

Microscopic examination of eyes, to which dichlorethylsulphide has been applied postmortem, shows no changes attributable to the action of the mustard gas liquid.

EYES OF ANIMALS RECEIVING SUBCUTANEOUS AND INTRAVENOUS INJECTIONS OF DICHLORETHYLSULPHIDE

Animals so treated died within five hours after the intravenous injection of one minim and uniformly, in four to five days after the subcutaneous injection of one minim. Microscopic examination of the eyes of these animals shows no evidence of conjunctivitis or other lesions.

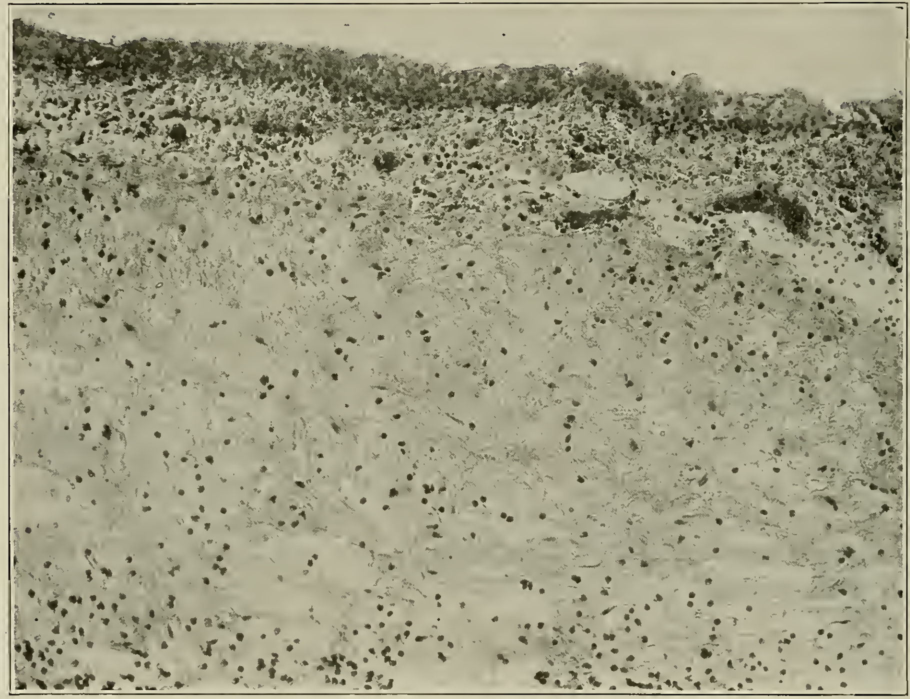

Fig. 82.—Section of palpebral conjunctiva eight hours after application of standard droplet. Complete necrosis of epithelium. Marked congestion. Minute hemorrhages. Polynuclear infiltration.

EYES SHOWING SECONDARY INFECTION

Four cases showing panophthalmitis, three at five weeks and one at six weeks, show microscopically a diffuse suppurative process involving all the structures of the eye and of the orbit. The suppurative process begins first in the cornea, and in the earlier stages may show as small pinpoint abscesses in the substantia propria, each surrounding a colony of cocci. The process extends through the anterior chamber toward the posterior portion of the eyeball until ultimately all is involved. Similar changes were observed in a dog three weeks after exposure, the earlier infection in this case resulting from the lack of care and the lessened resistance of this especial animal.

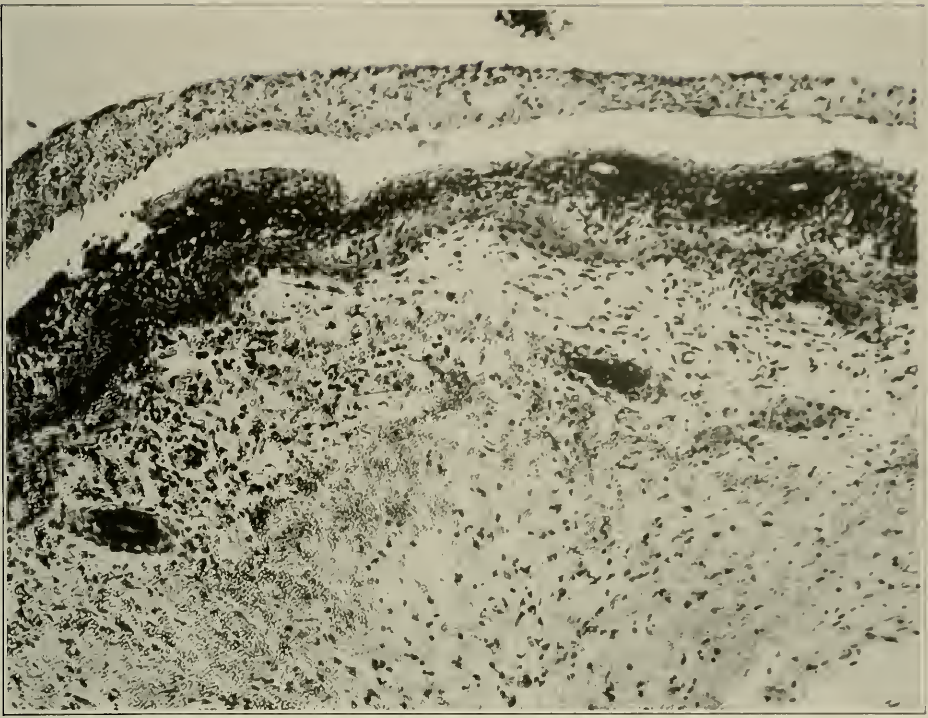

Fig. 83.—Section of palpebral conjunctiva just above the lid margin showing the fibrinopurulent exudate and greater degree of necrosis at this point.

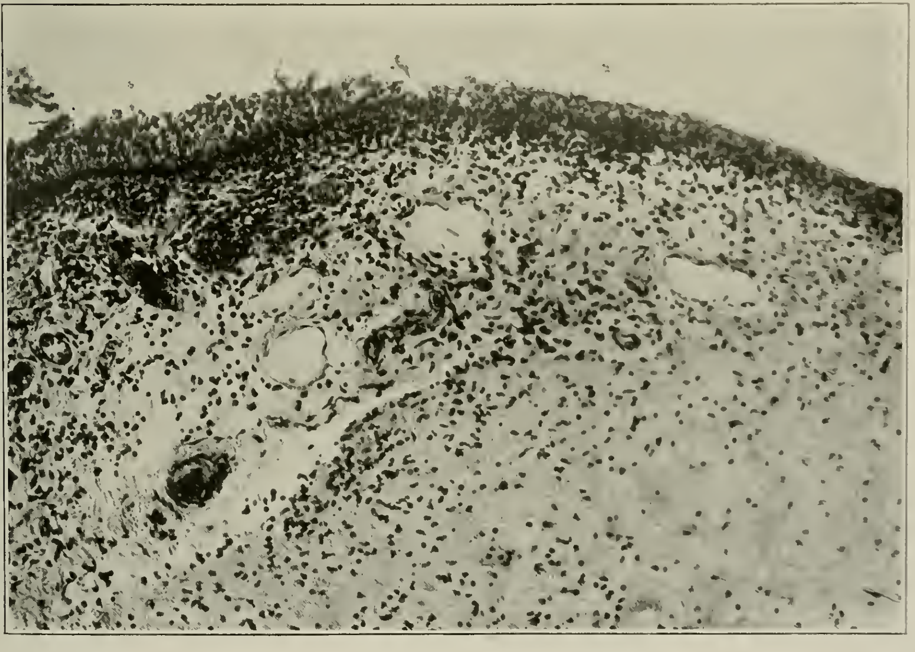

Fig. 84.—Palpebral conjunctiva twenty-six hours after application of standard droplet showing advancing necrosis, more marked infiltration, congestion, minute hemorrhages, and edema.

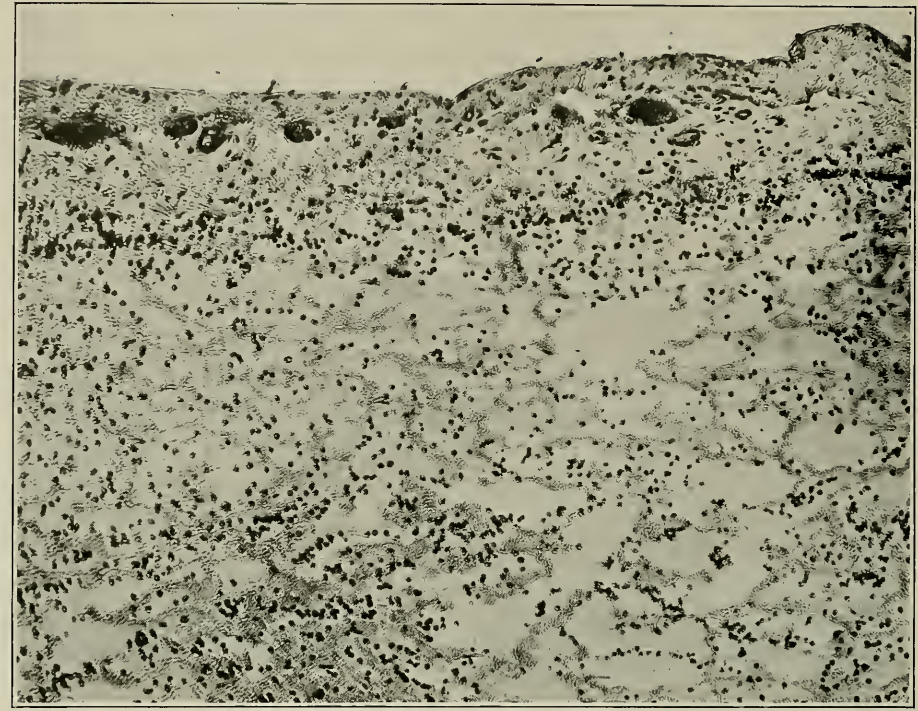

Fig. 85.—Palpebral conjunctiva thirty-four hours after application of standard droplet. Section at fornix of upper lid showing the complete loss of the necrotic surface, extreme edema and polynuclear infiltration.

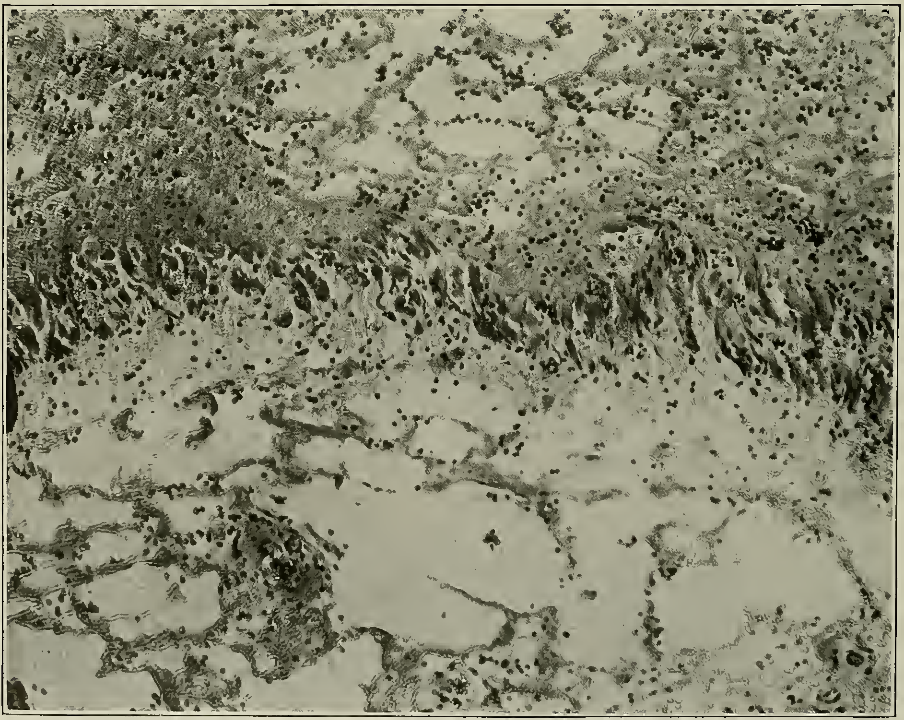

Fig. 86.—Section from the same region as in the preceding, but taken deeper down, showing the extreme edema and liquefaction necrosis, below the narrow band of the sphincter orbicularis.

CHANGES IN ORBITAL TISSUES

In the uninfected cases these consist of congestion and edema, and a mild diffuse inflammation, involving particularly the ocular muscles. In the infected cases there is a diffuse suppurative process.

Summary of the Microscopic Pathology

1. The microscopic changes produced by the direct application of the standard droplet of the liquid and by exposure for fifteen minutes to a vapor concentration of 1:20,000 are identical.

2. *Changes in the Cornea.*—The earliest changes noted are in the cornea, consisting of pyknosis and contraction of the epithelium and of the substantia propria, most marked at the corneal vertex and extending to Descemet's membrane. This is followed by a loss of nuclei until by the twelfth hour the corneal vertex shows complete necrosis, the necrosis often extending through the limbus nearly to the scleral junction. Desquamation of the dead corneal epithelium begins in about five hours. Polynuclear infiltration of the sclerocorneal junction begins in five to six hours. Fibroblastic proliferation was first noted at thirty-four hours at the sclerocorneal junction. Earliest signs of regeneration of the corneal substantia propria were noted at the periphery at sixty-five hours. New formation of blood vessels into the limbus was well marked as early as seven days. Slow repair of cornea continues for several weeks with development of a highly vascularized corneal cicatrix. Marked changes in the

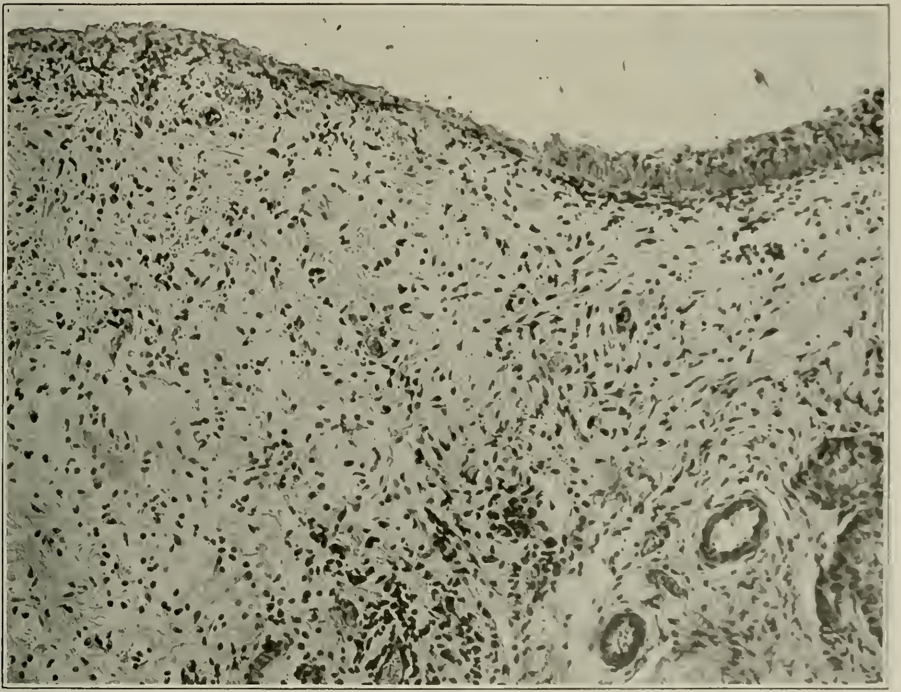

Fig. 87.—Section of upper lid at palpebral margin four days after direct application of standard droplet. Advanced ulceration, beginning repair.

corneal thickness occur as the result of separation of the lamellæ, edema, cellular infiltration and fibroblastic proliferation. The severity of the corneal lesion is in direct proportion to the concentration of the gas and the period of exposure.

3. *Changes in the Conjunctiva.*—Necrosis and desquamation of a large part of the conjunctival epithelium results, but it is noteworthy that this necrosis is much less in degree than that of the cornea or of the skin surfaces of the eyelids. The primary necrosis rarely extends beneath the basement membrane of the palpebral and bulbar conjunctiva, except at the palpebral margin where collections of a serofibrinopurulent exudate take place. Here shallow ulcers are produced. The most striking feature of the conjunctival involvement is the extreme edema of the subconjunctival connective tissues which is usually most marked in the bulbar conjunctiva near the scleral sulcus and in the palpebral conjunctiva of the upper lid. This is so extreme that liquefaction necrosis in this tissue, with marked leucocyte infiltration, usually follows. Petechial hemorrhages are of frequent occurrence in the subconjunctival connective tissue. Regeneration of the conjunctival epithelium occurs readily and healing takes place with a permanent thickening of the conjunctiva due to the formation of fibroblastic tissue.

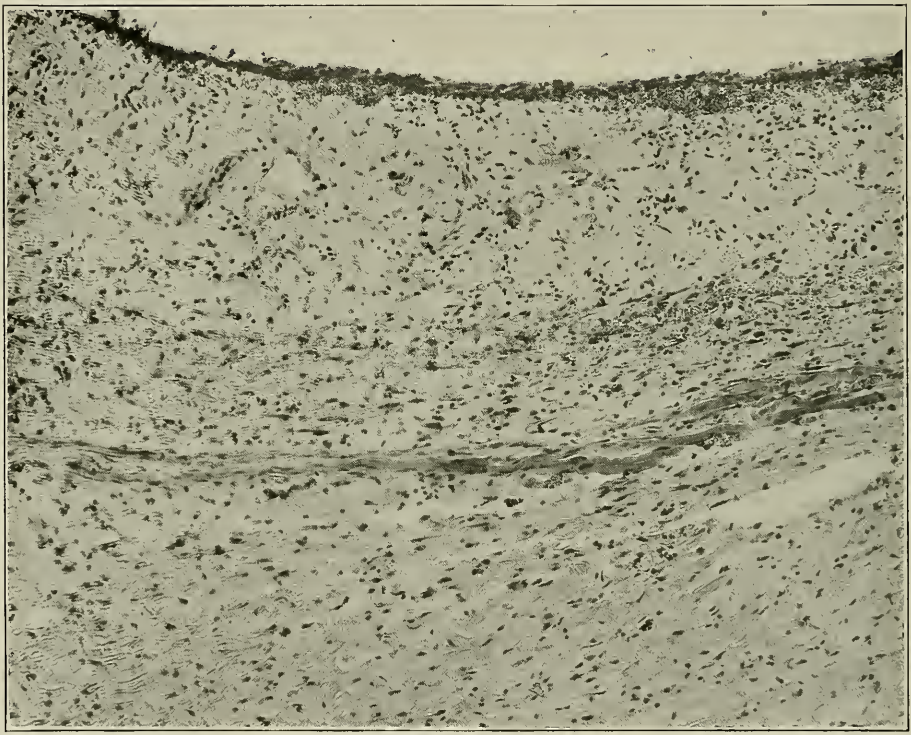

Fig. 88.—Section of same lid near fornix. Regeneration of the conjunctival epithelium. Disappearance of the edema and advancing cicatrization of the subconjunctival tissues.

4. *Structures of Eyeball.*—(See Figs. 99, 100.) Iritis and iridocyclitis with exudation into the anterior chamber, occur without infection in the severest

forms of gassing; and are common occurrences at about the third to sixth week in the uncared-for cases as the result of secondary infection even when the gassing was light. In the cared-for cases of average exposure, no changes were observed in iris, ciliary body, chorioid, retina and optic nerve, except congestion and edema.

5. *Nictitating Membrane.*—Changes observed in rabbits are necrosis of the epithelium, extreme edema, multiple hemorrhages, congestion, and eventually more or less marked thickening from connective tissue proliferation.

6. *Lacrimal Gland.*—Increased functional activity was noted at all times; ultimately, overuse atrophy and subsequent hypertrophy. Increased albumin content was observed in the secretion.

7. *Harder's Gland.*—Parenchymatous degeneration and inflammatory infiltration occurred.

8. *Tarsal Glands.*—Evidences of penetration into the tarsal glands were shown by degeneration and necrosis of certain of the acini. Leucocyte infiltration occurred about and into these glands.

9. *Skin Surface of Eyelids.*—The same changes were observed in the cutaneous surface of the eyelids as were described in the chapter on cutaneous lesions. The important influence of the sebaceous glands and hair follicles in permitting the entrance of the gas into the deeper tissues of the dermis is strikingly shown here, the penetration into and resulting escharization of the skin being greater than in the case of the cornea or the conjunctiva.

10. The relatively slight penetration into the subconjunctival tissues may be explained as the result of the protection afforded by the moistness of the surface and lacrimation.

11. *Orbital Tissues.*—In the cared-for cases congestion, edema and a mild diffuse cellular infiltration, particularly in the orbital muscles, were noted; in infected cases a diffuse suppurative cellulitis occurs.

III. Clinical Cases

(For the opportunity of examining the clinical cases, and for their histories, we are indebted to Capt. L. L. Roos.)

Case I.—(See Fig. 89.) Exposed to strong concentration of mustard gas vapor for 10 to 12 minutes. Patient wore a gas mask.

The eyes began to burn and be painful, lacrimated freely, and were red and inflamed two hours after exposure. Three to four hours after exposure he began to feel as though there were granules beneath the eyelid. He could not keep his eyes closed because there was much more pain when the lid borders were approximated. He was very sleepy, because of much loss of rest due to night work, and his eyelids felt heavy.

He went to bed. Boric acid compresses (cold) were applied. American oil was instilled once; it did no good. The compresses were to be continuous, they relieved the pain, but he could bear them only about one-half hour at a time, through the night. For three to four days argyrol was instilled once in 24 hours, and did very little good. The palpebral conjunctiva appeared "blistered" the morning after the exposure.

The irritation continued for three to four days but gradually decreased in severity. The congestion decreased but was still marked. In fact it was present and quite distinct thirty-one days after exposure.

The patient complained of ''misty'' blurring of vision which was marked at first and has decreased also, but was still present three weeks after exposure. The bright sunlight hurt his eyes, the lids felt heavy.

There was no interference with accommodation so far as the patient knew. He was able to read about the tenth day, but could only read a page at a time.

Examination.—Congested dilated vessels on the bulbar conjunctiva from the border of cornea, over the limbus, to the inner and outer canthus in each eye. The congestion and thickening of the bulbar conjunctiva showed in the palpebral aperture. The palpebral conjunctiva, especially superiorly, shows slight thickening.

Case II.—(Fig. 90.) Exposed ten to twelve minutes to a strong concentration of mustard gas vapor. He wore a gas mask at the time.

Sulphur dichloride and sulphur monochloride have always irritated his eyes. He first noted irritation under the arms about four hours after exposure, and just one hour later, that is, five hours after exposure, there was a stinging irritation ''just like salt'' in the eyes. One drop of ''Silvol'' solution was put in each eye. This increased the pain. The eyes lacrimated profusely, and the eye-balls were red, and the vessels congested. Boric acid compresses (cold) were applied at intervals all night. At 3 A.M he found that he could open his eyes only to a slight extent, the aperture was only about ½ inch at the greatest. The lids were edematous and this prevented the opening of the eyes. The morning after the exposure the eyes were completely closed and the lashes were ''glued together'' by the thick purulent exudate. He could not open the eyes wide enough to see anything. At the first-aid room argyrol and sterile American oil were put into the eyes and he was put to bed and cold or iced boric compresses were put on continuously for 5 days. Argyrol was instilled 3½ days after exposure for about 30 minutes and everything both near and far was found to be blurred. The conjunctiva was congested. For more than 10 days the eyes lacrimated profusely, especially the left eye. On the fifth day his vision was clearer but very much impaired. He could not distinguish letters at all on a printed page. He could not read ordinary print for ten days and then he could read the print for only 10 minutes at a time until the eyes ached, and things became blurred.

It was not until the eighteenth day that he could read for an hour at a time. His vision for distance has gradually improved but is still somewhat blurred. At the end of the third week near vision is such that he can as yet not read much more than one and a half hours at a time and then he must rest two to three hours.

Examination.—Thickening of the conjunctiva in the palpebral fissure is especially marked in the triangles with apex at the inner canthus and base at the inner limbus. The thickened conjunctiva is yellowish. The vessels are slightly congested. The palpebral conjunctiva is not very much changed, possibly slightly thickened.

Case III.—Exposure of 40 minutes in 4 shifts to strong concentration of mustard gas vapor while wearing a gas mask.

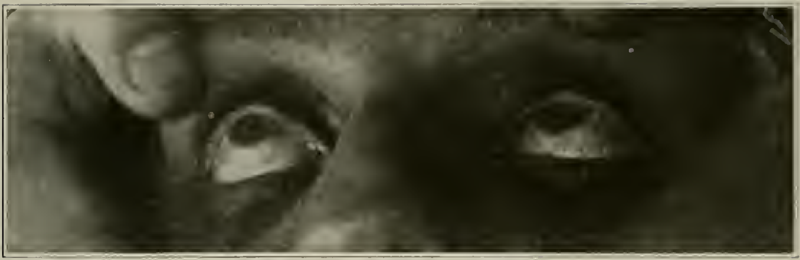

Fig. 89.—Congestion of the conjunctival vessels persisting to a marked degree, four weeks after exposure to dichlorethylsulphide vapor.

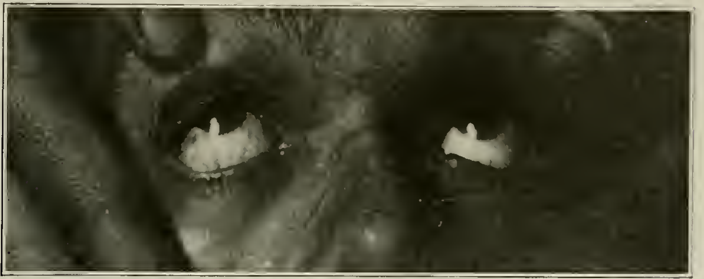

Fig. 90.—Persistent congestion four weeks after exposure to dichlorethylsulphide vapor. Acute symptoms were very severe and the patient still complained of dimness of vision when he left the hospital after five weeks.

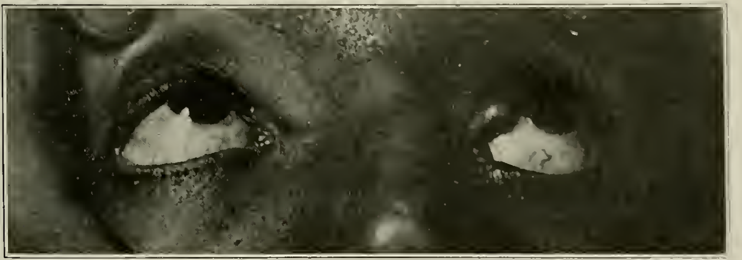

Fig. 91.—Marked conjunctival congestion and hordeolum of left upper lid in a case of severe mustard gas conjunctivitis. Four weeks after exposure. The hordeolum is a part of the general staphylococcus furunculosis which may characterize the later stages of the severe skin burns.

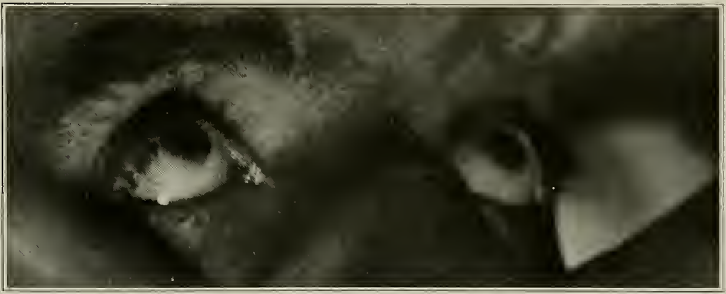

Fig. 92.—Dichlorethylsulphide conjunctivitis four weeks after exposure to vapor. In the acute stage there were extreme photophobia, lacrimation, pain, edema and purulent exudation. The residual congestion and seropurulent exudation are still evident.

The eyes had been congested for two days because of exposure to hydrochloric acid gas. On entering the infirmary at 6 P.M. he had no eye symptoms but because of the congestion the eyes were irrigated with sodium bicarbonate solution or boric acid. He was very nauseated and sick, and vomited, and retched very much. At the same time he complained of severe sharp pains in the eyes.

Boric acid compresses were applied continuously for three days and the eyes were washed with the boric acid about every fifteen minutes for the entire first night. The eyes were very painful, burned and felt as though an electric current was passing across and through the anterior part of the eye. The eyes were swollen and a purulent exudate glued the eyelashes down. On the third day while his eyes were being opened and argyrol instilled he had a flash of vision for a second, just long enough to see his nurse. On the fourth day he recognized individuals. He had been able to open his eyes about the fourth night, but he could only see a dull light. On the fifth day he opened his eyes slightly and everything was blurred; near and distant vision were equally impaired.

He was not able to read for about fourteen days, and then only for about five minutes at a time, gradually becoming able to read more and more, but at six weeks he can read only about one to two hours at a time. When in the sunlight, however, there is a feeling of ''wideness'' (of the palpebral opening), some blur, and some discomfort, and slight photophobia.

Examination.—In the morning there is slight purulent exudation which glues the eyelashes together; there is a small drop of purulent exudate in the inner canthus. There is a slight blepharitis marginalis. The ocular conjunctivæ show the thickened, slightly yellowish, elevated areas, pingueculæ, on either side of the corneæ. The vessels are large, slightly dilated and congested.

The palpebral conjunctiva shows nothing of any great interest.

CASE IV.—(See Fig. 91.) Exposure of 30 minutes to strong concentration of the vapor of dichlorethylsulphide while wearing the gas mask.

He was first exposed at about 3:30 P.M. and noticed his first symptoms at about 5 P.M. These were irritation, burning and lacrimation of the eyes and a ''faint feeling'' in the pit of the stomach. Then on leaving the infirmary and getting into ''the air'' the eyes felt better and he was not troubled until he returned to the infirmary. Here after taking the routine ''shower, kerosene rub and shower,'' treatment and retiring, his eyes felt very painful with the sensation of fine sand under the lids and there was profuse lacrimation. A thick serous exudate made the eyelashes mat together and seal the eye.

His vision was blurred, probably due to the increased lacrimatory secretion. The eyes were red and congested, according to his roommate. His eyes were irrigated with boric acid; American oil was instilled and cold boric acid compresses were applied continuously for five days. Argyrol was used from the second day until about the fifth day.

The eyes could not be opened, because the lids were swollen, edematous, and glued together at the margins by the matted lashes.

After the third day he was able to hold the eyes open for a few minutes at long intervals, but it was not until the fifth day that he could dispense with the compresses. His vision had been very blurred, but cleared fairly well on the fifth day. There was some yellowish exudation with considerable serous exudation. The eyes were washed frequently during the day with boric acid solution.

A hordeolum formed on the upper eyelid near the inner canthus, on about the fourteenth day.

The patient did not attempt to read for two weeks and when he did begin he noticed no trouble, except that the eyes ached after he had read a quarter to half an hour. He could not read magazines until about ten days later.

Examination.—The bulbar conjunctiva shows the same features as in the other cases but to a more marked degree; there is a thickening and a yellowish change, with marked congestion of the vessels of the part of the conjunctiva that is exposed in the palpebral fissures, on either side of the corneæ. At the limbic border a number of straight, small, deep vessels were seen to be injected and suggested a deeper penetration and a sclerociliary injection. The conjunctiva from the inner limbus to the inner canthus is more markedly involved.

Case V.—(See Fig. 92.) Exposed thirty to forty-five minutes in several shifts to strong concentration of dichlorethylsulphide vapor, while wearing gas mask.

Began on the evening shift at 4 P.M. and first exposed himself at this time. He noticed no eye symptoms until about 10 P.M. when there was burning, a feeling as though granules were under the lids, and a fairly profuse lacrimation. Cold boric acid compresses, boric acid eye washes, etc., were employed during the night and for several days. The routine treatment, as given, together with argyrol instillations was employed. According to the physician in charge, the patient was in severe shock.

There was some pain, blurred vision for near and distant objects, and a profuse lacrimation. At first the lacrimation was serous in type, but soon it became yellowish, thicker and almost purulent. The lids were tightly sealed and somewhat edematous.

The symptoms continued to be fairly severe and the treatment was kept up for about a week. It was not until this time that the vision was at all clear. The lacrimation continued for some time.

Examination.—Slightly congested areas in the palpebral aperture on each side of the cornea. The conjunctiva shows slight thickening in the same exposed areas. The discharge from the collection of the pus is found both in the inner and in the outer canthi. The palpebral conjunctiva shows nothing of significance.

Case VI.—(See Fig. 93.) Exposed 45 minutes in several shifts to strong concentration of mustard gas vapor, while wearing gas mask.

The irritation of the eyes began at about 9 P.M., some five hours after exposure. There was severe burning and a feeling of sand and glass scratching in the eyes.

There was profuse lacrimation and congestion. The next morning after the exposure the exudate from the eyes was seen to be more or less purulent and glued the eyelashes together, and held the eyes closed.

After the parts had been treated with cold boric acid compresses during the whole first night as had been done in all the cases it was necessary to "flush" the eyes with the solution in order to dissolve and loosen the plastic purulent exudate. When opened the eyes were found to be much congested and small blebs were seen, especially on the lower palpebral conjunctiva. Argyrol was instilled as in the other cases and continuous compresses were applied for five days. The eyes were opened for short spaces of time on the fourth and fifth days and a blurring and dimness of vision was noted.

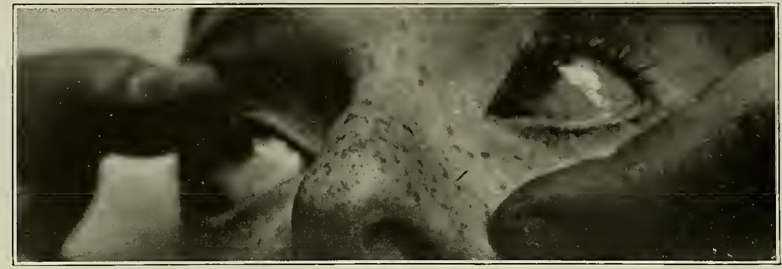

Fig. 93.—Dichlorethylsulphide conjunctivitis four weeks after exposure to vapor. The severity of the original process is indicated by the severe skin changes. The persistent congestion is the sole evidence of the severe conjunctivitis that was present.

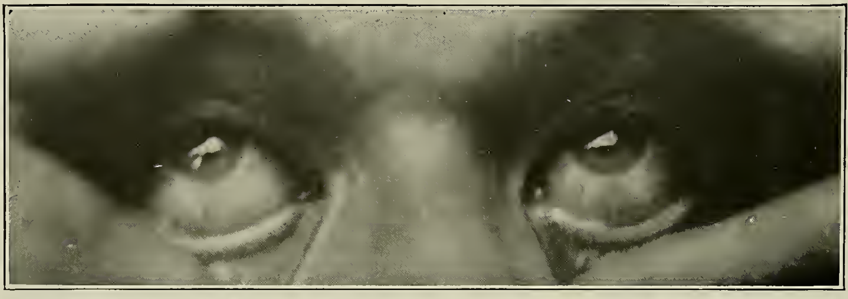

Fig. 94.—Repeated exposures to a low concentration of mustard gas vapor. Persistent congestion. Pigmentation of the sclera in the palpebral fissure. Yellowish pigmented elevation of the conjunctiva near inner segment of limbus of the nature of a pinguecula.

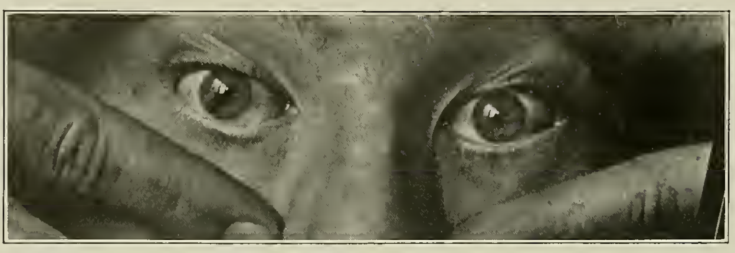

Fig. 95.—Conjunctival congestion and pigmentation of the sclera limited to the exposed area in the palpebral fissure of a patient subjected to low concentrations of mustard gas vapor over a relatively long period. Gave no history of a severe acute process.

Examination.—Shows the same condition that has been found in the other cases. The acute congestion has decreased and the signs remaining are those of a somewhat chronic irritative process. There is the slight thickening in the exposed part of the bulbar conjunctiva in the palpebral fissure.

CASE VII.—Exposed directly to strong vapor.

The vapor irritated the eyes severely and caused pain and lacrimation for ten to fifteen minutes. There were no blebs but there was some congestion. After this there was no more pain and the patient continued to work where there was practically always some vapor.

The patient's eyes were not painful but became more and more congested.

Examination.—The whole conjunctiva was inflamed, congested and slightly edematous, the lacrimation was increased in amount. The vision was apparently not involved. The bulbar conjunctiva was more markedly congested and affected than was the palpebral. Under the boric-acid-continuous-compress treatment, there was a decided improvement, the congestion was fairly well relieved in about four days.

On the fifth day the area which is most markedly injected is in the bulbar conjunctiva of the palpebral fissure. Some of the scleral vessels in this region are injected. The small subconjunctival fatty area (pinguecula) is present.

CASE VIII.—(See Fig. 94.) Exposed to fumes of ethyl alcohol, ethylene and some dichlorethylsulphide.

The eyes showed chronic irritation, thickening of the bulbar conjunctiva in the palpebral aperture, and some yellowish discoloration and areas that appeared to be fatty deposits.

The patient complains of impaired vision. He has had one severe arm burn but there were no eye symptoms at that time.

At present he complains of lacrimation and blurring of vision.

CASE IX.—(See Fig. 95.) There has been a slight irritation and itching and some congestion of the conjunctiva for about two weeks. At first the symptoms were very mild and noticeable only after exposure to dichlorethylsulphide. The symptoms were exaggerated and prolonged if the patient sat through a moving picture show. Bright sunlight also increased the symptoms.

The conditions have been more or less cumulative and the symptoms have gradually increased. During the past week, he has had lacrimation, congestion of the bulbar conjunctiva in the palpebral fissure and difficulty in accommodation in the right eye with more or less blurring of vision.

There is also some sticky seropurulent exudate, and in the morning the eyelids and lashes are glued together, and a drop of pus is seen in the inner canthus. He has used only the boric acid wash.

Examination.—Shows a picture similar to the others, with a thickening of the conjunctiva of the eyeball that is exposed in the palpebral fissure. The right eye shows slightly more congestion and thickening than the left and there is some ciliary injection about the sclerocorneal junction.

The palpebral conjunctiva, especially over the lower right eyelid, shows some congestion and slight thickening.

CASE X.—Exposure without mask to strong concentration of mustard gas vapor. Symptoms developed three hours later.

He complained of severe irritation and pain in the eyes and the lids were swollen, edematous and could hardly be separated. The routine cold boric acid compresses were used, and it was not until three days later that the edema disappeared.

Case XI.—Presented a somewhat different aspect. He was exposed for a short time, a few minutes, to quite a heavy dose of dichlorethylsulphide vapor. He had some slight irritation and lacrimation but no congestion to any marked degree. There was, however, a diminution of vision in the right eye which was said to be very marked. Both near and far vision were greatly reduced. There was blurring of all images.

Report of Eye Specialist.—"In regard to Case XI, whom I this day examined, I find his vision in right eye 4/200. Under atropine I find he has at least three diopters of hypermetropia with some astigmatism, the correcting of which does not improve his vision.

"If this condition has been brought about in the last three weeks as he claims, though the fundus does not show this, it must be toxic. Otherwise, it is amblyopic and his previous vision was not normal."

Case XII.—Has been exposed to dichlorethylsulphide for about one month. He had some irritation and congestion about one week ago. At present the condition appears to be much improved but the patient comes in complaining of failing vision, dimness and blurring. Both eyes are affected and the condition is progressing rapidly; both near vision and distant vision are involved. The patient must bring a printed page to within six inches of the eye in order to be able to read.

A close examination of the corneæ failed to reveal any opacities to account for the trouble. The corneal epithelium showed no apparent thickening or dulling. The conjunctiva shows some thickening and signs of chronic irritation in the part exposed in the palpebral fissure. It was considered that this case like Case XI was one of some internal fundus pathology or an accommodation disturbance.

Case XIII.—Exposure of 1 hour to very dilute concentration of mustard gas vapor.

Six hours later marked burning and irritation of conjunctiva, lacrimation, blurring of vision and reddening of conjunctival surfaces. These symptoms lasted three days and gradually decreased, but a feeling of roughness of lids and visual disturbance persisted for nearly two months.

Clinical Summary

From these cases it will be seen that exposure to varying concentrations of vapor of dichlorethylsulphide for varying periods produces a conjunctivitis showing all stages and degrees of intensity from a simple acute type to a severe chronic proliferative conjunctivitis. The symptomatology and clinical picture may vary greatly. The lesions are most marked in that portion of the bulbar conjunctiva exposed in the palpebral fissure. The milder cases recover after several days or weeks, but the more severe cases develop chronic hyperemia of the conjunctiva, new formation of vessels and scar tissue in the most severe, with more or less permanent disturbances of vision. One of the cases observed developed an almost complete amblyopia in one eye, so that only the perception of light and shadows was possible. In another case marked bilateral gradual reduction of vision was noted. A xanthoma-like pigmentation was also noted in the chronic cases, the pigmentation developing near the outer or inner sclerocorneal junction, or over the corneal limbus.

There is no evidence of any metastatic involvement of the eye. In cases showing severe burns of other parts of the body, arm, leg, etc., no conjunctivitis, even of the simplest type, developed. Such exceptions are explained entirely by the fact that the vapor did not reach the eyes externally. In other cases with severe burns over the entire body with the exception of the face, which was protected by the gas mask, no eye or conjunctival symptoms were noted.

IV. Treatment

Inasmuch as the routine and universally employed clinical treatment accorded the cases, as described above, seemed to us unsatisfactory, experimental investigation was carried out with a hope of obtaining some improved method of treatment applicable to human cases. The use of Dakin's solution in the eye was naturally contraindicated because of its too great irritating properties, so that milder chlorinating solutions were sought for this purpose and the choice naturally fell upon the solution of dichloramine-T in chloreosane, particularly as this substance had been recommended by various writers for the treatment of infective conditions of the eyes, such as trachoma. Our experiments showed that this solution, if applied to the eye before exposure to the gas, has a definite prophylactic action, and that when applied before and after exposure the resulting lesions are much less severe. (See Figs. 96, 97, 98, 99, 100.) In cases in which the exposure extends over a period of several hours, the administration of dichloramine-T in chlorcosane causes, naturally, no change in the intensity of the lesion. Here its after-use is indicated for its germicidal action, and the prevention of secondary infection. It seems to us likely that instillations of dichloramine-T in chlorcosane solutions could be used as prophylactic methods on the battlefield during a known gas attack, and that in cases

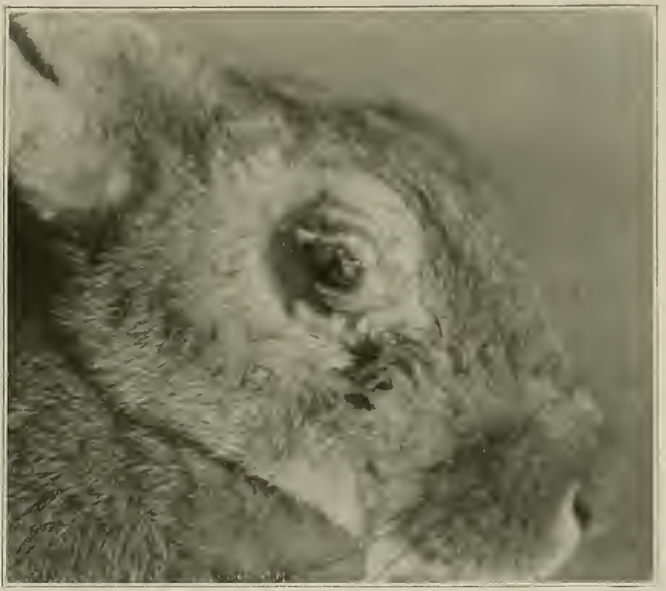

Fig. 96.—Five weeks after direct application of dichlorethylsulphide to cornea. Dosage about twice the size of the standard droplet. Lids not separated. Eye untreated. Resulting purulent panophthalmitis with collapse of eyeball.

of severe eye injury due to dichlorethylsulphide its use should be continued for the purpose of preventing secondary infection.

SUMMARY OF TREATMENT

1. The use of any method of treatment which brings pressure upon the lids and eyeball such as tight bandaging or heavy compresses is absolutely contraindicated.

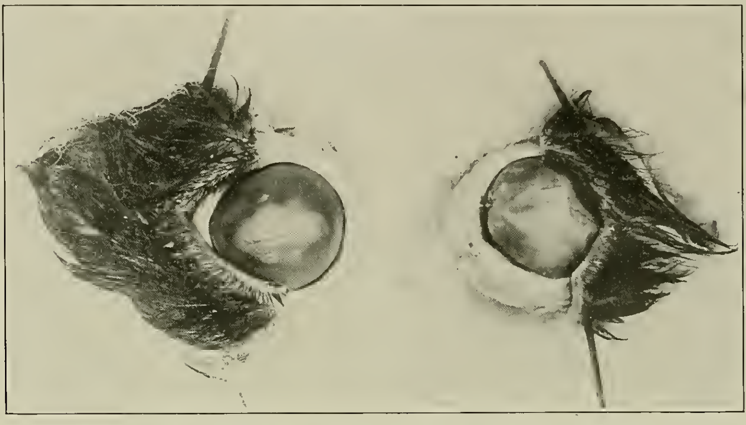

Fig. 97.—Right and left eyes of a rabbit 92 hours after 12 hours' exposure in gas chamber to a concentration of 1:50,000 of dichlorethylsulphide. Right eye received prophylactic treatment with dichloramine-T, 0.5 per cent in chlorcosane. Left eye untreated. Right eye shows much less marked corneal necrosis, the area of necrosis being sharply demarcated by the somewhat approximated borders of the palpebral fissure. The characteristic line described by Pissarello shows beautifully. The left eye shows the usual diffuse necrosis of the cornea.

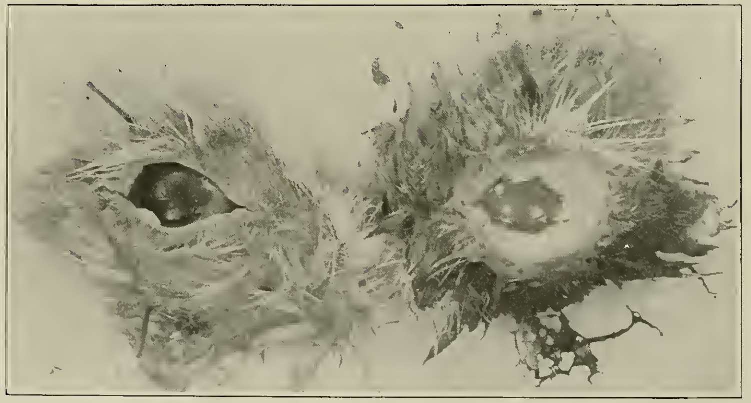

Fig. 98.—Right and left eyes of rabbit gassed at the same time as the preceding. Right eye treated with four applications during the first 36 hours of dichloramine-T, 0.5 per cent in chlorcosane. Died 96 hours after end of exposure. Right eye shows less edema and much less marked corneal injury; left untreated for 60 hours, at end of which time some purulent exudate formed. Left eye, entirely untreated, showed the usual marked edema and corneal necrosis, with marked purulent exudation.

2. For the mild cases, frequent irrigation with saturated boracic acid, the use of light weight boracic acid compresses, hot vapor baths, and protection of the eyes by darkening of the room, or by a light gauze bandage or by the use of smoked goggles are recommended.

3. Special care must be taken to prevent the gluing together of the eyelids by accumulation of the exudate. Should this occur the exudate should

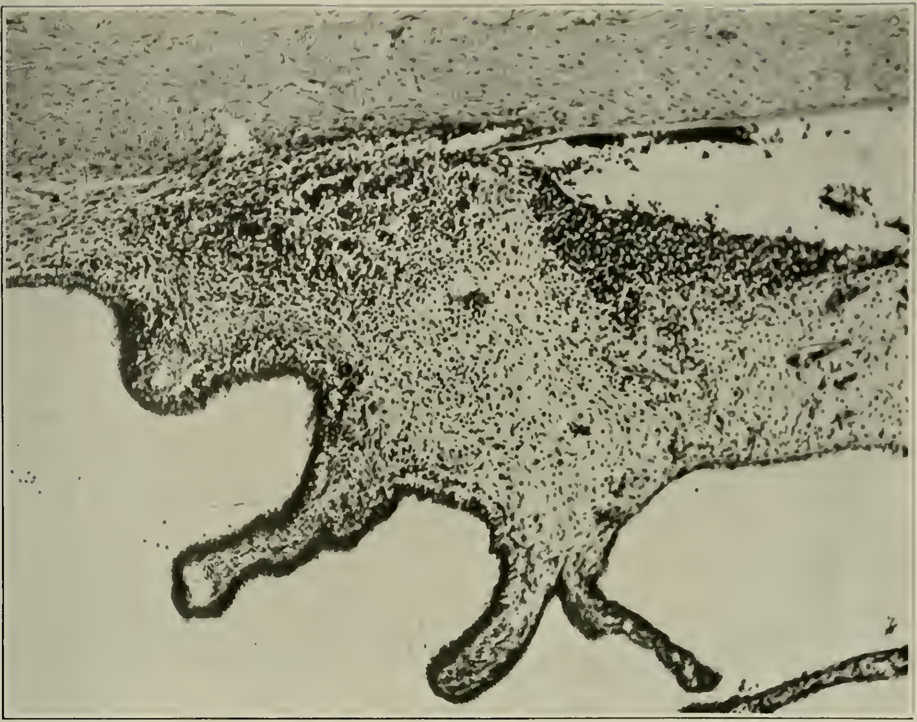

Fig. 99.—Ciliary body from eye of rabbit exposed 12 hours in gassing chamber to a concentration of 1:50,000. Animal died 92 hours later. Marked collection of polynuclear leucocytes in anterior chamber, in the ciliary body, and in the iris of the left eye which had received no treatment with the dichloramine-T solution. Same rabbit as in Fig. 97.

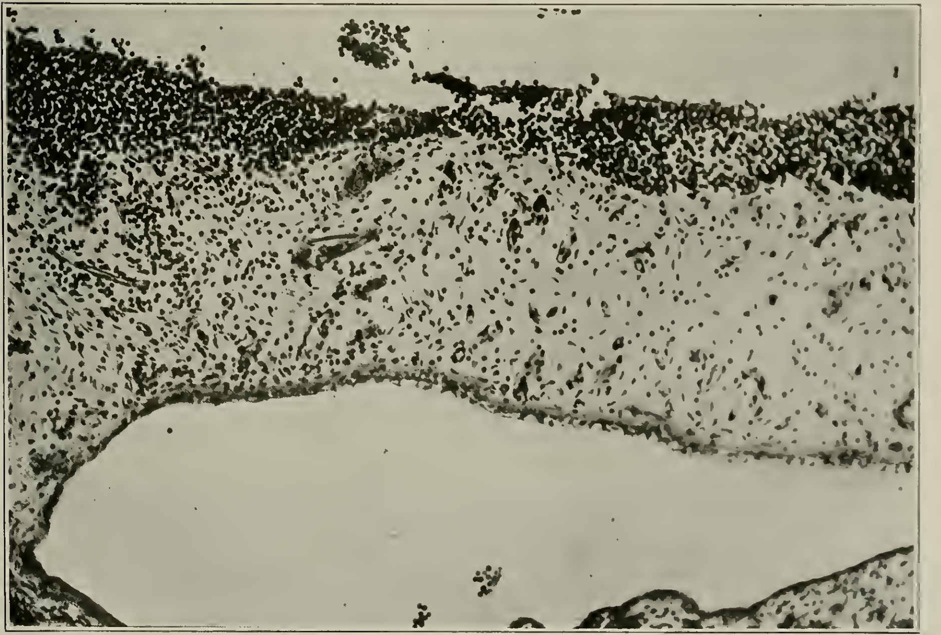

Fig. 100.—Iris of same eye as in preceding figure, showing congestion, edema and polynuclear infiltration. Marked polynuclear exudate in the anterior chamber.

be softened and washed away with boracic acid with care to avoid forcible separation of the lids.

4. The use of argyrol, silvol, etc., is in our opinion, undesirable.

5. The use of cocaine is considered unwise.

6. For the severe forms the use of a 1 per cent Dakin's solution is found to be too irritating. We therefore recommend the employment of the chlorcosane solution of dichloramine-T in a strength of 0.5 to 1 per cent, or even stronger. We further advise that in all cases of exposure to mustard gas this solution be used as an immediate irrigant for its prophylactic effects, followed in the milder cases of injury by boracic acid irrigation and in the severe cases by repeated irrigations with the dichloramine-T solution for the prevention of secondary infection.

7. For the treatment of the refractive errors and more permanent disturbances of vision the patient must be referred to a competent ophthalmologist.

Conclusions

1. The action of mustard gas upon the cornea and conjunctiva is essentially the same as that upon the skin. The conjunctiva is, however, less susceptible to the action, or better protected, as the degree of necrosis produced in it is always less than that in the cornea or the epidermis.

2. Exposures to dilute concentrations of the vapor produce slight degenerations of the corneal and conjunctival epithelium followed by a simple conjunctivitis. The use of a 2 per cent alkaline aqueous fluorescein solution in demonstrating the necrosis of the corneal epithelium within ten to fifteen minutes after exposure to gassing has great clinical value.

3. Exposures to stronger concentrations produce a more or less complete necrosis of the corneal vertex, extending throughout the entire depth of the cornea. Purulent exudation into the anterior chamber may occur; but no changes except congestion and edema were observed in the posterior chamber or optic nerve in noninfected cases. In severe cases iridocyclitis and iritis may occur without secondary infection. The conjunctival epithelium also suffers necrosis, and there results an intense edema of the subconjunctival tissues with marked congestion, multiple hemorrhages, leucocyte infiltration, and frequently secondary liquefaction necrosis. The depth of the necrosis in the conjunctiva is much less than that in the palpebral epidermis. This difference in degree of escharization can be explained in part by the penetration of the hair follicles on the skin surface, and in part by the moistness of the conjunctival surfaces and the lacrimation. A diffuse mild inflammation of the peribulbar tissues occurs, often with marked infiltration of the ocular muscles. Purulent panophthalmitis may result from secondary infection, but is rare.

4. No metastatic lesions of the eye could be produced experimentally by applications of mustard gas to other regions of the body, or by subcutaneous or intraperitoneal injections.

5. For the milder forms of mustard gas conjunctivitis we recommend immediate irrigation with the 0.5 to 1 per cent chlorcosane solution of dichloramine-T followed by frequent irrigation with saturated boracic acid solution; for the severe forms the same initial treatment followed by frequent irriga-

tions with the dichloramine-T alternating with boracic acid. We advise against the use of bandages or compresses bringing pressure upon the eye, against the use of colloidal silver preparations, and against the use of cocaine. During exposure to mustard gas vapor the dichloramine-T solution may be used as a prophylactic agent.

6. Healing in the more severe forms results in vascularization and cicatrization of the cornea with marked disturbances in vision. Even in the milder forms of conjunctivitis, localized roughness or irregularity in the conjunctival surface may persist for weeks as the result of localized edema, hyperemia, cellular infiltration, etc. Serious refractive errors and reduction of vision result, even in mild cases. For the correction of the disturbances of vision the patient should be referred to a competent specialist.

NOTE.—Since the publication of the above, an article on the "Effects of 'Mustard Gas' on the Eyes," by *G. S. Derby*, Am. Jour. Med. Sc., 1918, clvi, p. 733-736, gives brief and incomplete clinical notes on mustard gas lesions of the eyes, without adding anything new.

CHAPTER IV

THE LESIONS OF THE RESPIRATORY AND GASTROINTESTINAL TRACTS PRODUCED BY MUSTARD GAS (DICHLORETHYLSULPHIDE)

I. Lesions of the Respiratory Tract

That irritation and inflammation of the upper respiratory tract, terminating in pneumonia, can be experimentally produced in animals by mustard gas was demonstrated in 1886 by *Victor Meyer,* the discoverer of this chemical entity. After its introduction into military use by the Germans, in the present war, the irritant effects of mustard gas upon the mucous membranes of the respiratory tract were noted by medical observers in the Allied Armies. The earlier British Army reports describing the respiratory symptoms produced by exposure to mustard gas speak of an initial tendency to sneeze, with gradually increasing nose and throat irritation, followed in about twelve hours by a free discharge of mucus from the nose. Prolonged exposures, even to slight concentrations, were observed to cause laryngitis and aphonia, even severe enough to put the men out of action. In the more severe cases bronchitis and pneumonia were found to develop thirty-six to forty-eight hours after the exposure. Ulceration of the mucous membranes of the respiratory passages may be so extensive and severe as to cause death in itself or a fatal bronchopneumonia may follow. About 95 per cent of the men gassed with mustard gas showed involvement of the respiratory tract.

Giraud (*Journal de Médecine et de Chirurgie Pratiques,* 1917, lxxxviii, 890) found that symptoms of involvement of the respiratory tract in the form of aphonia, coughing, tracheitis and bronchitis were, next to the eye lesions, the most common affections produced by exposure to mustard gas. *Mandel and Gibson* (*Journal American Medical Association,* 1917, p. 247) describe the respiratory symptoms of mustard gassing as an ''irritative, noninflammatory, nonfebrile'' laryngitis and bronchitis, with a feeling of constriction about the larynx, tightness of the chest, aphonia, and paroxysmal cough, particularly severe at night, with a serous discharge in the mild cases, hemorrhagic expectoration in the most severe, and purulent in the late stages complicated by bronchopneumonia. The physical signs are those of a diffuse bronchitis. The chief complications are pulmonary edema and a relatively late bronchopneumonia.

Pissarello (*Giornale di Medicina Militare,* 1918, lxvii, p. 128) describes the respiratory affections in mild cases of mustard gassing as coryza, dryness of throat and hoarseness, while in the more severe cases the hoarseness may pass into complete aphonia, with congestion and tumefaction of the pharyngeal mucosa, swollen uvula, and spots of whitish-gray exudate over the pharyngeal mucosa. He noted a laryngotracheitis only in the most severe cases, with occasional extension to the bronchi, with râles, or the production of atelectatic areas. In only two cases did he find a bronchitis with subfebrile state.

Rendu (*Lyon Médical*, March, 1918, p. 108) gives the most complete clinical description of the lesions of the upper respiratory tract caused by exposure to mustard gas, with a series of figures showing the location of the lesions in the nose, pharynx and larynx. The nasal symptoms were coryza lasting from one to five days, with a serous discharge, and epistaxis in one-eighth of his cases, and very frequently a diminution or complete loss of the senses of taste and smell. Rhinoscopic examination showed usually only a congestion of the mucosa, but in some cases small whitish ulcers were present at the level of the anteroinferior portion of the septum, or at the head of the inferior turbinate. The chief symptom referable to the pharynx was dysphagia, appearing usually about the second to third day and lasting about four to six days, but in some cases more severe and of longer duration. The objective symptoms were redness of the mucosa accompanied by a turgescence of the uvula and the posterior pillars. In about 15 to 20 per cent of the cases seen, localized whitish diphtheritic necroses were noted upon the pharyngeal mucosa, particularly upon the uvula and the neighboring borders of the pillars, but also on the posterior pharyngeal wall in its median portion, or behind the posterior pillars. In the most severe cases the diphtheritic eschars covered the entire posterior wall of the oropharynx and the laryngopharynx. Rendu found laryngotracheal symptoms to be the most common manifestation of the action of mustard gas in the upper respiratory tract. The subjective symptoms were sensations of tickling, dryness or burning, localized in the region of the larynx and behind the sternum, lasting for several days or weeks according to the intensity of the lesions of the mucosa. Coughing was constant and very painful, appearing about the same time as the laryngeal symptoms just described; it was dry, paroxysmal and was most troublesome at night. In about one out of ten cases there was for several days a blood-streaked expectoration. The voice was rough or husky in 60 to 70 per cent of cases, and a complete aphonia occurred in about 30 to 40 per cent. The vocal symptoms disappeared very slowly as a rule. Rendu observed no symptoms of laryngeal spasm or edema. The laryngoscopic examination showed changes in the laryngeal mucosa ranging from a more or less marked hyperemia, accompanied by a tumefaction of the arytenoids and ventricular bands and the folds of the posterior commissure, to the development of whitish eschars, like those in the pharynx, localized at different places in the mucosa. He describes the development of the eschars as follows: During the first three or four days only the hyperemia of the mucosa is noted; the laryngoscopic examination is often difficult because of the abnormal intensity of the pharyngolaryngeal reflexes. From the fourth to the seventh day the necrosis of the mucosa begins to show in grayish or whitish patches resembling a false membrane. These eschars were observed most frequently at the vertex of the arytenoid pyramids, the border of the epiglottis, and the free border of the vocal cords, associated as follows: epiglottis and arytenoids, cords and arytenoids, and epiglottis, cords, and arytenoids. The most frequent lesions of all were the isolated eschars of the vocal cords which were arranged symmetrically on the anterior two-thirds of the free borders of the cords in the form of an elongated segment, sharply delimited on its external border, but somewhat irregular on its internal. The eschars are creamy white in color, while the remainder of the cord is deep red. The healing of these lesions is very slow, and requires several weeks. The *tracheal* lesions are analogous to those of the larynx; their subjective symptoms are more or less confounded with those of a bronchitis so often coexistent.

In the few reported autopsy findings in cases of death resulting from mustard gas the lesions of the respiratory tract are not very fully described. *Canelli,* in one case, observed a diffuse tracheitis, bilateral subacute bronchitis, pulmonary hypostasis with acute diffuse edema, and a localized fibrinoadhesive pleuritis. *McNee,** in summing up autopsy findings, states that the respiratory tract lesions were acute inflammation of the air passages, desquamation of the mucous membranes and formation of false membrane, to which may be added infection in the form of acute purulent bronchitis, with atelectasis and bronchopneumonia. Emphysema may also be present. *Dunn*† in four autopsies found the chief lesions to be severe damage to bronchi and bronchioles, persistent edema, and severe infection of respiratory tract, bronchopneumonia, and in two of the cases, hemorrhagic exudations. *Karsner* (*American Journal of Medical Sciences,* 1918, clv, 904) noted the following respiratory lesions in four autopsies following death from mustard gassing: Mucous membranes of nose and pharynx were the seat of a marked mucous inflammation. Larynx, trachea and bronchi showed severe inflammation, in one case with pseudomembrane formation, in two others with multiple necroses of the mucosa. In two cases there was an acute fibrinous pleurisy. All cases showed a bilateral bronchopneumonia with slight general edema of the lungs. *Rendu* records that in two autopsies the laryngotracheal mucosa, completely necrosed, was detached in shreds like a false membrane.

The animal experiments of *Kolls* and *Gilbert, Raper* and *Ball, Marshall* and *Miller,** and others have shown that mustard gas produces in exposed animals coryza, pharyngitis, salivation, tracheal rattle, congestion of the tracheal mucosa, bronchitis and bronchopneumonia. In the *United States Naval Bulletin,* April, 1918, there are some color plates of the gross pathologic changes in trachea and larynx of a dog dying forty-eight hours after a thirty-minute exposure to a 0.13 milligram-liter concentration of mustard gas. Edema and congestion of epiglottis and glottis, and an acute membranous tracheitis are shown. A section of lung from another dog shows atelectasis and patches of focal pneumonia following a thirty-minute exposure to 0.056 milligram-liter concentration. Plate V shows similar tracheal and pulmonary conditions.

The pathologic changes in the respiratory tract described above are chiefly those noted in clinical and gross pathologic observations. At this time no published reports in the general literature exist in which the detailed microscopic pathology of the respiratory tract lesions of dichlorethylsulphide gassing is given. It is the object of this investigation to present such a statement of the minute pathology of these lesions, in such a way as to give a complete picture of the process from the mildest type of lesions to the most severe.

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*For references, see Bibliography at end of Chapter II.
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METHOD

In our gassing investigations we have made use of a simple apparatus, which has served our purposes most effectively and is to be recommended for its simplicity, as well as for the relative accuracy with which the gas concentration can be estimated. As shown in Fig. 101, it consists of:

A, one or more bottles containing sulphuric acid for drying the air admitted.

B, a container for the liquid mustard gas so arranged as to be easily detached from the tubing, so that when stoppered with a ground glass stopper, it can be weighed with its contents. Above this is a shunt tube for varying the amount of pure air admitted to the chamber, thus varying the concentration of gas obtained. Within the mustard gas bottle strips of absorbent paper are so arranged as to increase the evaporation surface. When used for experimental work with toxic substances, which are gaseous at room temperature, the gas intake replaces this weighing bottle.

C, a gassing chamber which is large enough to hold several small animals or a large dog. It has a removable plate glass top, so that the animals can be observed during gassing; this is sealed during the experiment with the gutta-percha-tallow mixture, commonly used for making air-tight seals for museum jars, and may be held in position by a heavy weight, if necessary.

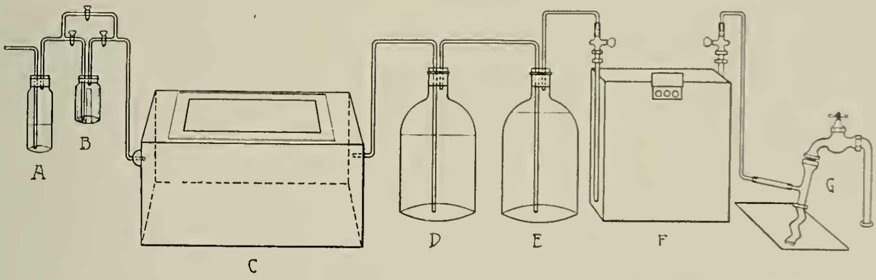

Fig. 101.—Experimental Gassing Apparatus. (Pathological Laboratory—University of Michigan.) A, Washer containing sulphuric acid; B, Gas container; C, Gassing box; D and E, Degassing bottles; F, Standard gas meter; G, Suction pump.

D and *E,* bottles for removing the gas from the air flowing from the chamber, so that the amount passing over can again be estimated here if desired. When used for mustard gas these bottles may contain a chlorinated solution for the destruction of the gas.

F, a standard gas meter for measuring the amount of air passing through the chamber.

G, a suction pump attached to the city water supply.

After detaching the weighing bottle air is drawn through the gassing chamber for some time in order to wash out the mustard or other gas remaining. The weight of mustard gas used is obtained by difference and the amount of air drawn through during the period in which the bottle is attached is recorded from the gas meter. The concentration represented by these figures is obtained by reference to a transformation table. The results are as approximately correct as can be obtained by any other form of gassing chamber, and the apparatus has the advantage of simplicity. As far as mustard gas is concerned, such factors as variable absorption by the hair of the animal, etc., introduce unavoidable errors, so that absolute accuracy of method can not be obtained, regardless of the limitations of the apparatus.

The animals were killed by a direct blow upon the neck to avoid the changes in the respiratory system produced by an anesthetic. Autopsies were made as quickly as possible after the death of the animal. The tissues were fixed in formol, embedded in paraffin; and the usual stains, hematoxylin and eosin, etc., were employed.

Gross and Microscopic Pathology

Various series of animals were exposed to varying concentrations of mustard gas in the gassing chamber for varying periods of time. It was found that rabbits would survive a forty-minute exposure to a dilution of 1:110,000, recovery taking place after a period of respiratory involvement. For purposes of brevity typical protocols have been selected and are given here.

Rabbit 32.—Exposed in the gassing chamber for forty minutes to a 1:110,000 concentration. During the gassing the rabbit frequently changed position, rubbed its nose, and showed signs of irritation. When removed from the gassing chamber the rabbit appeared unaffected in any way. In two and one-half hours conjunctival erythema and increased lacrimation were evident, these symptoms increasing until the animal was killed. Seven and one-half hours after removal from the box, symptoms of coryza manifested themselves. Twelve hours after removal from gassing chamber, rabbit was killed by blow upon the neck. The conjunctivæ presented marked congestion and edema, and were covered with purulent flakes. The bulbar conjunctivæ showed a marked collar of edema at the limbus. The cornea showed a slight haziness, and at its vertex there was a definite necrosis of the superficial epithelium. This area was irregularly oval in shape. The lid margins showed marked congestion and the skin about mouth and nostrils was erythematous.

Autopsy showed right-sided dilatation of the heart. No fluid was found in the pleural cavity, and there were no pleural changes. On section the lungs showed marked congestion and edema without hemorrhages or atelectasis visible to the naked eye. No differences between upper and lower lobes were noted. The trachea was filled with frothy mucus and the mucosa was congested, particularly in the upper portion, the congestion diminishing below toward the bronchi. The mucosa of the entire upper respiratory tract, nose, mouth, pharynx and larynx showed congestion without hemorrhages.

Microscopic Findings.—Nose. Sections from the skin about the nostrils show slight pyknosis of the epidermis and congestion of the vessels, without other changes. The mucous membrane of the nose shows a marked congestion, more marked pyknosis of the epithelium and slight edema. Sections from the *pharynx and larynx* show a marked congestion with extreme mucous degeneration of the mucous glands. There is pyknosis of the upper layers of epithelium of the mucous membrane but no definite necrosis. The acini of the mucous glands are greatly enlarged and filled with deep blue-staining mucus. The ducts are dilated and filled with mucus. There is but slight edema of the mucous membrane and no hemorrhages. These signs diminish in the *trachea* except for the edema, which is somewhat greater in the lower part of the trachea than above, and there is an increased number of wandering cells in the mucosa. The columnar cells of the tracheal mucosa show more marked changes than the squamous epithelium of the upper respiratory tract. The great majority show a hydropic or a mucoid degeneration. The epithelium is intact for the greater part but small patches of desquamation occur. The larger *bronchi* present the same appearance as the trachea, though to a somewhat lesser degree. The smaller bronchi are filled with mucus. The epithelium shows mucoid degeneration and occasional areas of desquamation. The walls of the larger bronchi are edematous, the vessels markedly congested, but there is no increase in leucocytes. The exudate in the bronchi is entirely mucoid or albuminous in character, not fibrinous. There is no hemorrhage into the bronchi. The *lung* tissue shows extreme congestion and

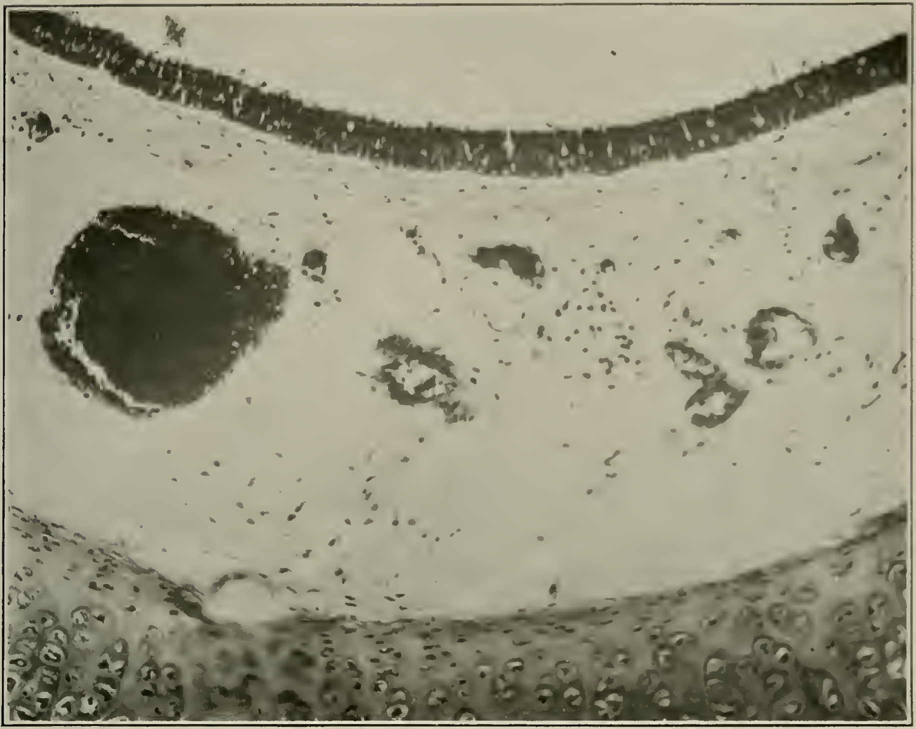

Fig. 102.—Section of laryngeal mucosa, Rabbit 31. Exposed thirty-five minutes to a concentration of 1:30,000. Killed thirty hours after gassing. Pyknosis and mucoid degeneration of the epithelium. Marked congestion and edema of the submucosa.

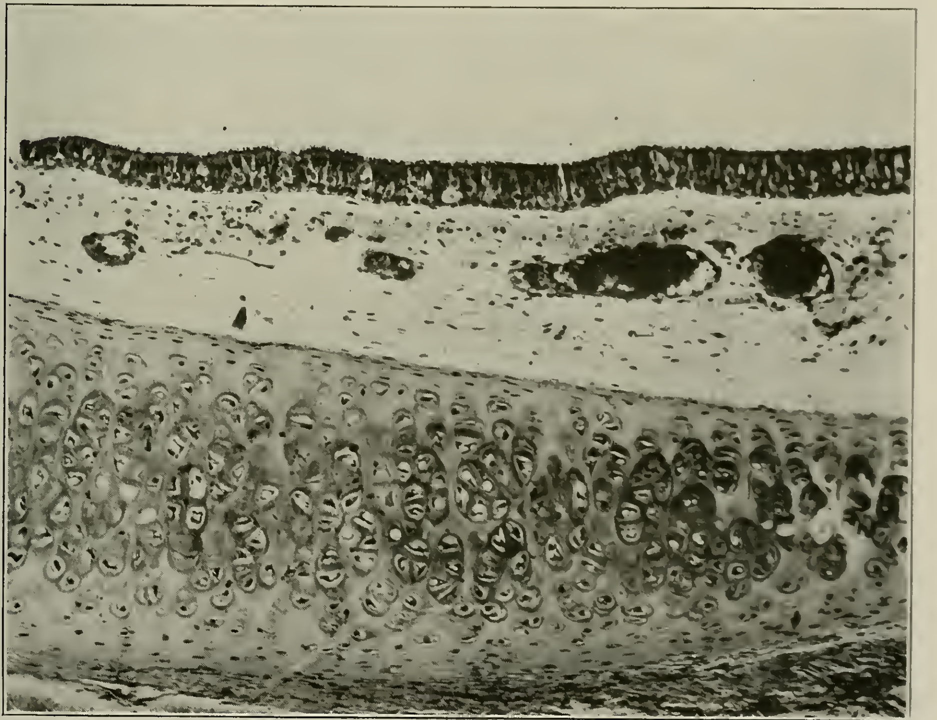

Fig. 103.—Section of tracheal wall of same rabbit as Fig. 102. Similar changes in epithelium and submucosa.

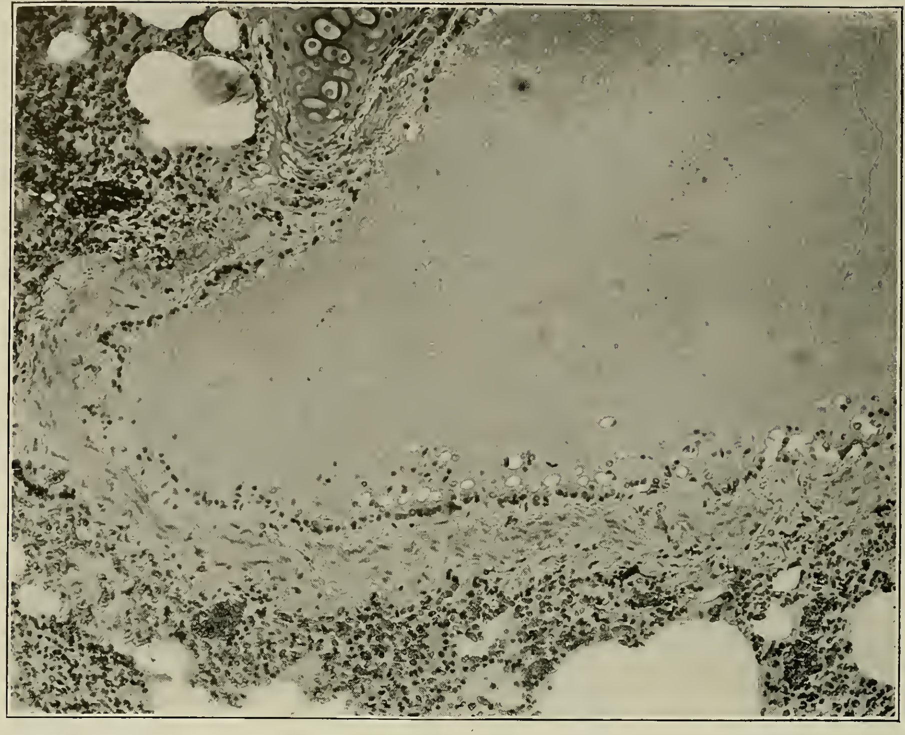

Fig. 104.—Rabbit 30. Exposed thirty minutes to a concentration of 1:15,000. Killed four and one-quarter days after gassing. Section of larger bronchus showing lumen filled with edema fluid. Bronchial epithelium shows marked mucoid and hydropic degeneration.

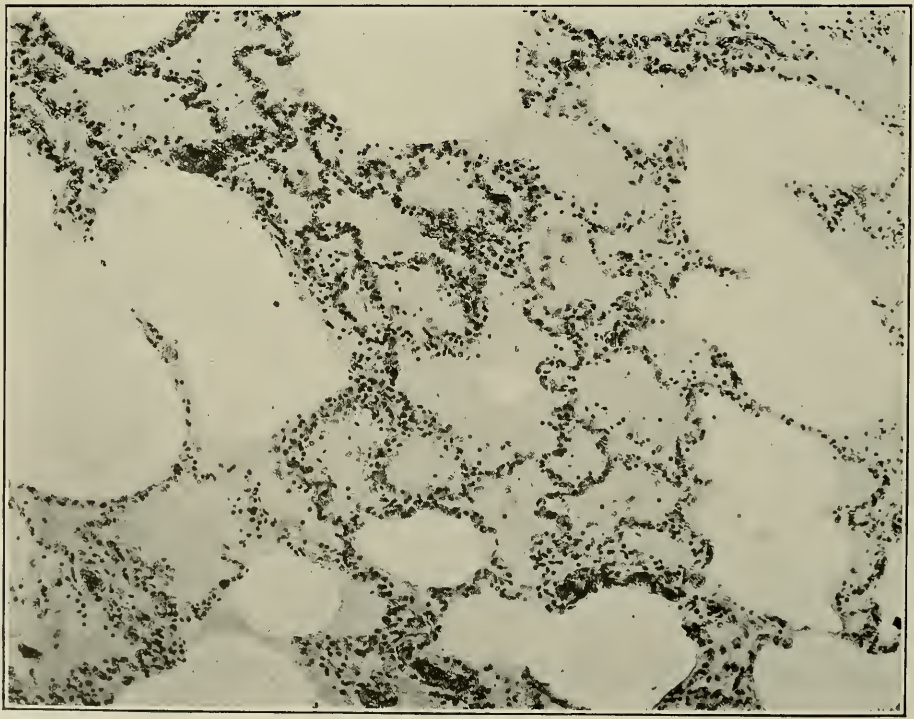

Fig. 105.—Lung of same rabbit as Fig. 104. Acute congestion and edema.

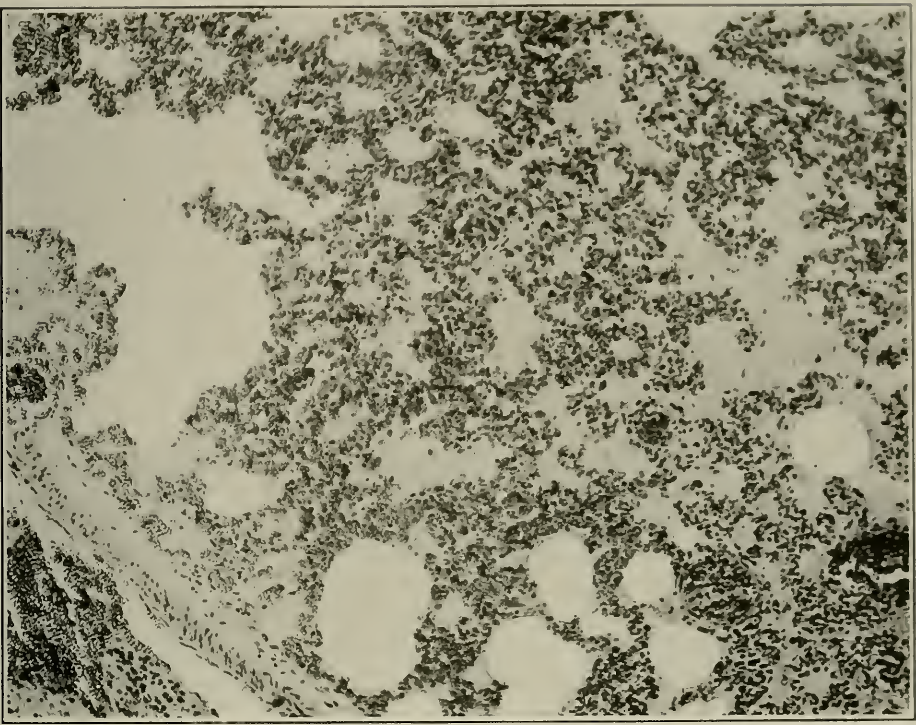

Fig. 106.—Rabbit 32. Exposed forty minutes to a 1:110,000 concentration. Killed twelve hours after removal from gassing chamber. Section of lung. Marked congestion, edema, and areas of partial atelectasis alternating with those of emphysema.

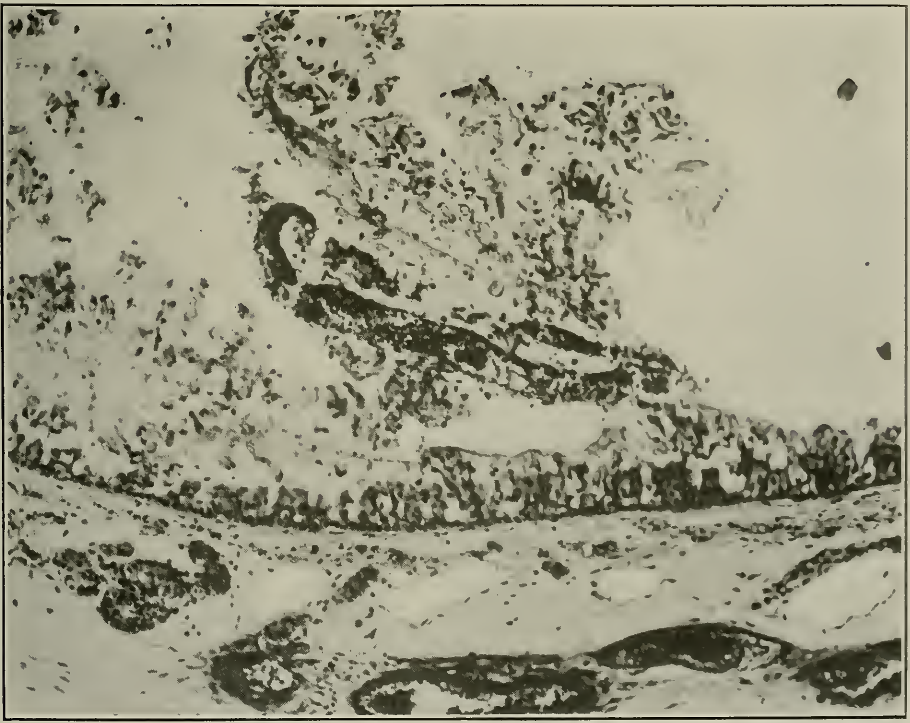

Fig. 107.—Rabbit 33. Exposed twenty minutes to a concentration of 1:15,000. Killed thirty-six hours after gassing. Section of trachea showing acute catarrhal desquamative tracheitis; marked mucoid degeneration of the epithelium; congestion and edema of the submucosa. Lumen filled with mucus containing many desquamated cells.

marked edema, with numerous minute hemorrhages, too small to be seen with the naked eye (See Fig. 106). A majority of the alveoli are filled with a heavy albuminous precipitate, but scattered throughout the lung are numerous emphysematous alveoli and dilated bronchioles. No areas of complete atelectasis are seen, although edematous areas show partial collapse.

The changes in the respiratory tract of this animal are those of an acute catarrhal rhinitis, pharyngitis, laryngitis, tracheitis and bronchitis, decreasing somewhat in intensity from above downwards, with pulmonary congestion and edema.

Rabbit 33.—Exposed twenty minutes to a concentration of 1:15,000. During the exposure the rabbit changed its position from that of facing the inflowing mustard gas to the opposite direction. Three hours after removal from the gassing chamber the animal showed increased lacrimation in both eyes. The borders of the eyelids, skin areas about the mouth and nostrils, the ears and all parts of the body where the hair was short and thin exhibited a marked erythema. The animal showed marked photophobia and irritation of the eyes. Eight hours after removal from the chamber flakes of purulent material were seen over the conjunctivæ and a definite coryza had developed. The conjunctivæ were edematous and congested. These symptoms increased for thirty-six hours, when the animal was killed.

Autopsy showed a severe conjunctivitis and coryza. Right-sided dilatation of the heart. The upper air passages were filled with foamy exudate and the mucosa was congested. Pleural cavities and pleuræ negative. The lungs were markedly congested, the right lung more so than the left. The lungs appeared air-containing throughout, except for the middle lobe on the right, which was solid in areas, dark red in color. On section it bled but slightly. Beyond congestion no other changes were found in any organs or tissues.

Microscopic Findings.—The cutaneous borders of the *nostrils* show necrosis, edema, congestion and marked leucocyte infiltration of the corium. The mucous membrane of the nose presents patches of necrosis of the epithelium, congestion and edema, areas of small-celled infiltration of the submucosa, and marked mucous degeneration of the mucous glands. *Mouth and pharynx.* Sections of tongue and pharyngeal wall show a contraction of the upper half of the squamous epithelium with pyknosis of the nuclei, congestion of the vessels, slight edema of the submucosa and slight small-celled infiltration. The *larynx* presents patches of necrosis in the hyperemic mucous membrane with marked edema extending to the cartilages. Small-celled infiltration is well marked. Mucous glands show marked mucoid degeneration. The surface of the mucosa of the *trachea* is covered with patches of mucus containing desquamated cells. The epithelium shows marked mucoid and hydropic degeneration; there are large areas of complete necrosis with desquamation. In the submucosa there is a marked edema extending to the cartilage rings. The vessels are markedly congested (see Fig. 107). The larger *bronchi* show marked degeneration and necrosis, and desquamation of the epithelium, the epithelium being represented for the greater part by a single line of nuclei at the base. Many of the bronchi are filled with an exudate of mucus containing many desquamated and degenerating cells but few leucocytes. There is some edema of the walls of the bronchi and the number of leucocytes is increased around the bronchi. The smaller bronchioles show a better preserved mucous membrane but many of the cells are vacuolated, presenting mucoid or hydropic degeneration, and desquamation is frequent. The *lung* shows practically the same picture as in the preceding; marked congestion and edema, small hemorrhages into the alveoli and emphysematous alveoli and dilated bronchioles. Many of the edematous areas show partial atelectasis. The apparently solid area from the right lung presents a more marked atelectasis and a greater degree of edema but no pneumonia. Other organs show marked congestion without other changes.

The microscopical picture in this case is similar to that in the preceding, but the changes are somewhat greater in intensity with a greater degree of necrosis and a well defined leucocyte reaction.

RABBIT 30.—Exposed thirty minutes to a concentration of 1:15,000. Killed four and one-quarter days after removal from the gassing chamber. Within five minutes after removal from the box the animal showed the first signs of irritation, rubbing its eyes and nose frequently. Six hours afterwards there was a well-developed conjunctivitis. By twenty-four hours the conjunctivitis had greatly increased with marked conjunctival edema, and the animal showed a marked bilateral coryza. By the second day the snuffles and coryza were much worse, the animal showing a marked respiratory wheezing, audible several feet away. The conjunctivitis had become distinctly purulent in character, with multiple subconjunctival pinpoint hemorrhages, extreme edema and beginning corneal ulceration. Throughout the day the snuffles and wheezing greatly increased, the animal appeared sick, restless, with respirations greatly increased and shallow, these symptoms reaching their height in the evening of the second day. From the morning of the third day the respiratory symptoms gradually improved until the animal was killed, four and one-quarter days after gassing.

Autopsy.—The eyes showed a very severe purulent conjunctivitis with characteristic porcelain appearance of the cornea. The mucosa of upper respiratory tract showed marked congestion and edema and mucous exudate diminishing in intensity from the nostrils to the nasopharynx. In the anterior two centimeters of the nasal tract the exudate was purulent in character. The nasopharynx, larynx and trachea presented marked congestion of the mucosa, and the lumen of the trachea was filled with a frothy mucus extending into the bronchi. No hemorrhages or ulcerations were seen in the mucosa of the upper respiratory tract. Pleural cavities and pleuræ were negative. The lungs were uniformly markedly congested and apparently air-containing throughout. No pneumonic areas or hemorrhages could be felt or seen. The heart presented a marked right-sided dilatation. Beyond a marked congestion, other organs and tissues showed nothing.

Microscopic Findings.—Nose. Sections from the anterior nostrils show a marked necrosis and ulceration of the mucosa with a marked edema and congestion of the submucosa and a polynuclear infiltration. Great numbers of staphylococci are seen on the necrotic mucosa. Throughout the submucosa are numerous minute hemorrhages by diapedesis, and in one medium-sized blood vessel, a definite thrombus. The mucous glands of the nose and nasopharynx present intense mucoid change. Sections from the *pharynx* show the squamous epithelium to be intact for the greater part, but the outer half is necrotic, dry, looking like stratum corneum. *Larynx.* The surface epithelium is completely necrotic in many areas, particularly where a mucoid exudate lies upon the surface. In other areas it is preserved, but has lost its columnar appearance, and is reduced to a layer of pyknotic nuclei staining almost black with hematoxylin. In the mucoid exudate in the lumen there are great numbers of swollen desquamated mucoid epithelial cells and very few leucocytes. The submucosa is edematous, the edema, however, being very irregularly distributed. The blood vessels show marked congestion and the number of leucocytes in the submucosa is not increased. The laryngeal mucous glands show marked mucoid degeneration. Many of the larger *bronchi* are filled with mucus. The columnar cells show marked mucoid degeneration and pyknosis. Practically every cell is converted into a goblet cell. There is no increase of leucocytes in or about the bronchi. The pulmonary vessels show extreme congestion and in many of these are large masses of fibrin, irregularly scattered through the red blood cells, or at times somewhat laminated, presenting the appearance of recent thrombosis. Throughout the *lung* atelectatic areas alternate with emphysematous. The alveolar spaces of the atelectatic areas show marked edema, being filled with a pink-staining finely granular precipitate. The bronchioles in these atelectatic areas are distended and are filled either with a similar edematous fluid or a more mucous fluid. No pneumonic areas are found and no large hemorrhages. Minute hemorrhages by diapedesis are found along the walls of the greatly distended capillaries. The other organs show nothing but intense congestion. (See Figs. 104, 105.)

The lesions are practically the same as in Rabbit 33, except that they are more severe in the nose and mouth. The purulent character of the nasal lesions is probably to be explained by the development of a secondary infection due to a staphylococcus.

Rabbit 31.—Exposed thirty-five minutes to a concentration of 1:30,000. On removal from the gassing box the animal showed some irritation of the eyes and nose. Four hours after removal the animal had developed a well-marked conjunctivitis with erythema of the exposed skin surfaces, and beginning snuffles with scant nasal secretion. Within twenty-four hours there was marked increase of the conjunctivitis and coryza. The animal was killed thirty hours after gassing.

Autopsy.—Eyes showed a marked conjunctivitis with purulent exudate. Exposed skin surfaces showed erythema and edema. The mucosa of entire respiratory tract from nose to bronchi showed congestion, slight edema, and abundant mucous exudate. Pleural cavities negative. Pleuræ negative. Lungs presented uniform congestion without consolidation, the lung tissue being apparently air-containing throughout. No hemorrhage or atelectatic or pneumonic areas visible to the naked eye. The heart showed dilatation of the right side. In other organs nothing notable but congestion.

Microscopic Findings.—Nose. Squamous epithelium of the anterior nostrils shows patches of complete necrosis, these minute erosions or ulcerations being covered with a fibrinopurulent exudate. The remaining epithelium shows more or less pyknosis. There is very little edema of the submucosa and no small-celled infiltration or hemorrhages. On the skin side of the nostrils the edema is more marked than on the mucosal side, and there is marked necrosis, pyknosis and desquamation of the epidermis. *Pharynx.* Squamous epithelium of mouth and pharynx shows patches of pyknosis, contraction of the upper third with pyknosis of the nuclei resembling cornification, congestion of the blood vessels and slight edema of the submucosa. *Larynx.* The columnar epithelium shows marked mucoid or hydropic degeneration. The majority of the cells of the upper layer are either vacuolated or are goblet cells. The nuclei stain very heavily, but the epithelium is for the greater part intact, without desquamation. In the lumen there is a thin albuminous fluid containing very few desquamated cells, leucocytes, no fibrin, and but a small amount of mucin. The submucosa shows a rather marked edema with the leucocytes slightly increased. The vessels are markedly congested. The mucous glands show increased mucus formation. *Trachea.* The epithelium is intact throughout the greater portion, but shows mucoid and hydropic degeneration. The lumen is filled with a thin mucoserous fluid. Well-marked edema of the submucosa with some increase in leucocytes. Marked congestion of the vessels. *Bronchi.* The lungs present practically the same appearance as in the previously described cases but with less edema and on the whole a less marked congestion. The bronchi contain a smaller amount of fluid. The epithelium is better preserved, although showing mucoid change and vacuolar change in the larger ones. There is very little atelectasis, the *lungs* being rather emphysematous throughout. There is no pneumonia and no hemorrhage. The other organs show chronic congestion, the liver a chronic coccidiosis with cirrhosis. (See Figs. 102, 103.)

In this rabbit the lesions in the anterior nares are severe, the degree of necrosis there being comparable to that on the conjunctiva and cornea, but the laryngeal, tracheal and bronchial lesions are of the mildest degree.

Rabbit 46.—Gassed six hours at a concentration of 1:50,000. Animal died sixty hours after removal from the gassing chamber. During the gassing the animal showed irritation within half an hour. At the end of an hour it became drowsy and was quiet with its eyes half closed. Within three hours there was a definite lacrimation and conjunctival edema, these conditions increasing during the remainder of the gassing. When taken from the box the eyes were very much congested, edematous and showed profuse lacrimation. By the next day the rabbit showed marked respiratory involvement, coughing all the time, and bubbling râles could be heard throughout its chest. These conditions increased during the next two days, the animal dying sixty hours after removal from the gassing chamber.

Autopsy.—Both eyes presented marked corneal opacity with mucopurulent conjunctivitis. Pharyngeal mucosa very markedly congested and edematous and covered with mucopurulent exudate. Buccal mucosa negative in appearance. Marked edema of all laryngeal structures and tracheal mucosa, the tracheal edema being most marked in the upper part, just beneath the larynx, where there were also small hemorrhages in the mucosa. Pleural cavities and pleuræ negative. Pericardial fluid increased, clear. Heart dilated; both sides filled with partly clotted blood. Both lungs were voluminous and air-containing without any airless areas except a small atelectatic area in the border of the lowest left lobe. On section the lungs showed moderate congestion and edema without any hemorrhages or pneumonic or atelectatic areas visible to the naked eye. Other organs showed no changes except congestion.

Microscopic Findings.—Nose. Anterior nares show a shrinking and pyknosis of the epithelium, the outer layers being desquamated and light staining, resembling cornified epithelium with pyknotic nuclei. In many areas this pyknosis and shrinking extends to the lowest layer of the epithelium. Through the lowest layer there are many hydropic cells and occasionally small vesicles are formed. The ciliated columnar epithelium shows a more marked necrosis, vacuolization and desquamation. There is marked edema of the submucosa extending to the cartilages and through the muscles. The mucous glands show extreme mucoid degeneration; the blood vessels, extreme congestion. There are minute hemorrhages about the mucous glands and the number of wandering cells is increased. The *buccal mucosa* and the *tongue* show necrosis of the upper half to two-thirds of the squamous epithelium, with partial desquamation of these dead cells in lamellæ. There is slight edema and moderate congestion of the subepithelial tissues. The mucosa of the *pharynx* shows the same changes with a more marked edema of the submucosa. *Larynx.* In the lumen, lying upon the surface, there is a fibrinopurulent membrane which is firmly attached in areas where the epithelium is completely lost. In these areas the picture is that of a diphtheritis. Colonies of staphylococci are present in the diphtheritic membranes and on the necrosed epithelium. Where the epithelium is preserved it shows marked vacuolation with hydropic and mucoid degeneration. In some areas the epithelium is still attached but is necrotic and infiltrated with polynuclears and eosinophile cells. There is a very marked subepithelial edema, extreme congestion of the blood vessels and areas of leucocyte infiltration, many of these being eosinophiles. This infiltration is most marked in the neighborhood of the diphtheritic areas. The cervical lymph nodes in this case show marked eosinophilia and great numbers of hemophages in the sinuses. *Trachea.* Mucosa of the trachea shows marked mucoid and hydropic degeneration. There is a diphtheritic necrosis, but the process is less marked than in the larynx. Edema and congestion of the wall are about the same. The epithelium of the larger *bronchi* shows marked degeneration and necrosis. There is an increase in leucocytes in the walls of the larger bronchi, the submucosa is edematous and the vessels are markedly congested. The majority of the smaller bronchioles contain a mucopurulent exudate and the bronchial wall is infiltrated with leucocytes. Around many of the bronchioles there are definite areas of a hemorrhagic purulent bronchopneumonia. Colonies of staphylococci are found in each of these areas. Between these areas the alveoli are overdistended and emphysematous. Other alveoli contain a heavy albuminous precipitate of edema. The *liver* presents a marked nutmeg liver, central necrosis and congestion of lobules. The *kidneys* show marked cloudy swelling and congestion. (See Figs. 110, 111.)

The respiratory lesions in this animal are more pronounced than in any of the preceding, as is shown by the diphtheritic necroses in the larynx and trachea, the purulent bronchitis and bronchopneumonia. The cause of death is considered to be an infective (staphylococcus) bronchopneumonia, secondary to the lesions produced by the gassing.

Rabbit 45.—This rabbit was gassed at the same time as Rabbit 46, in the same box for six hours at a concentration of 1:50,000. Its reaction during the gassing and afterwards appeared to be identical with that of No. 46, but the animal lived for seven days.

Autopsy.—The autopsy findings were the same as for No. 46, but the changes were more severe in character. The anterior nares showed extensive ulcers covered with diphtheritic membrane and the nasal cavity was filled with a mucoid fibrinopurulent

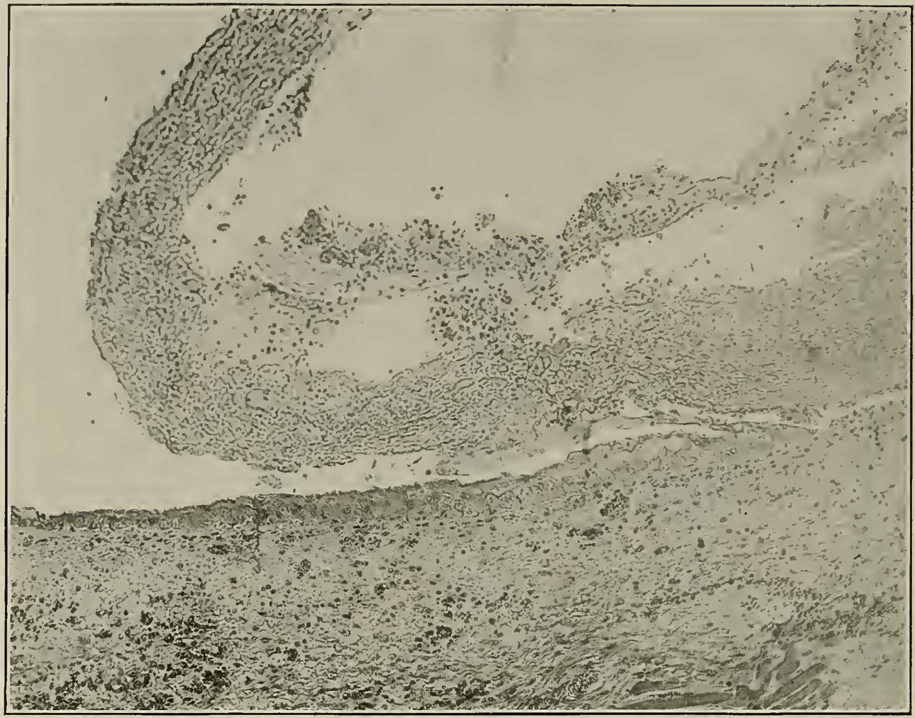

Fig. 108.—Rabbit 43. Exposed twelve hours to a concentration of 1:50,000. Died fifty-four hours after exposure. Section of tracheal wall, showing pseudomembrane in lumen and complete necrosis of the surface epithelium.

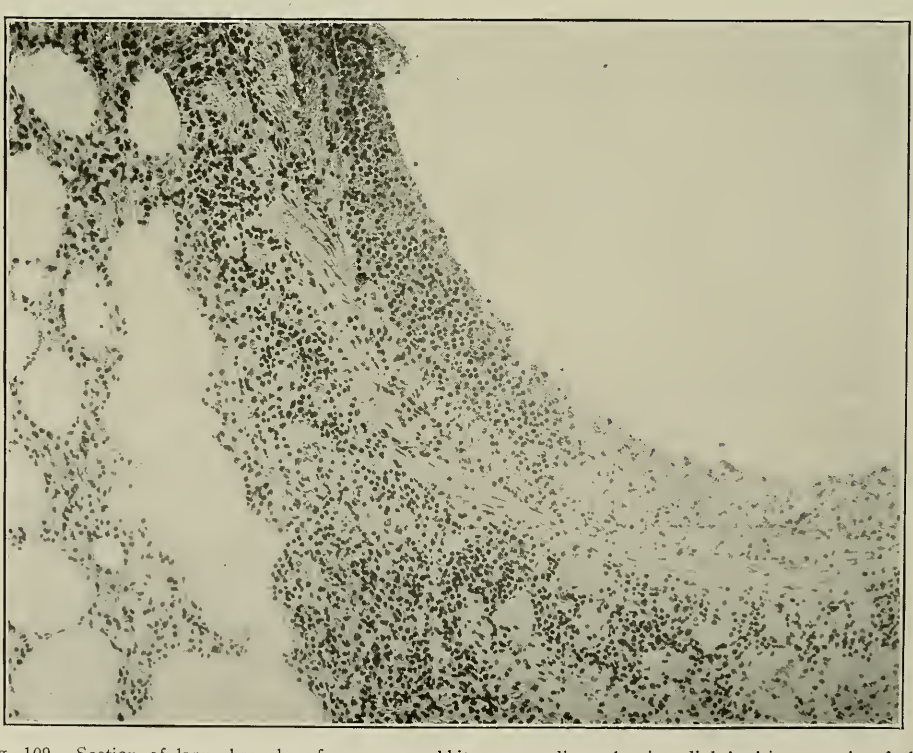

Fig. 109.—Section of large bronchus from same rabbit as preceding, showing diphtheritic necrosis of the mucosa. Early bronchopneumonia.

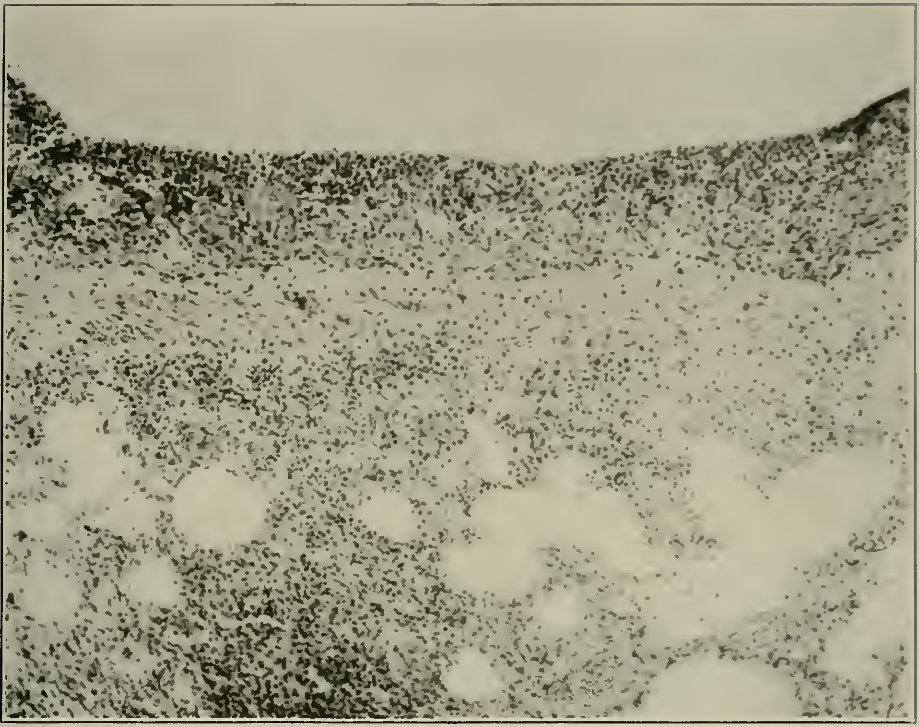

Fig. 110.—Rabbit 46. Exposed six hours to a concentration of 1:50,000. Died sixty hours after gassing. Section of large bronchus, showing purulent necrotic bronchitis.

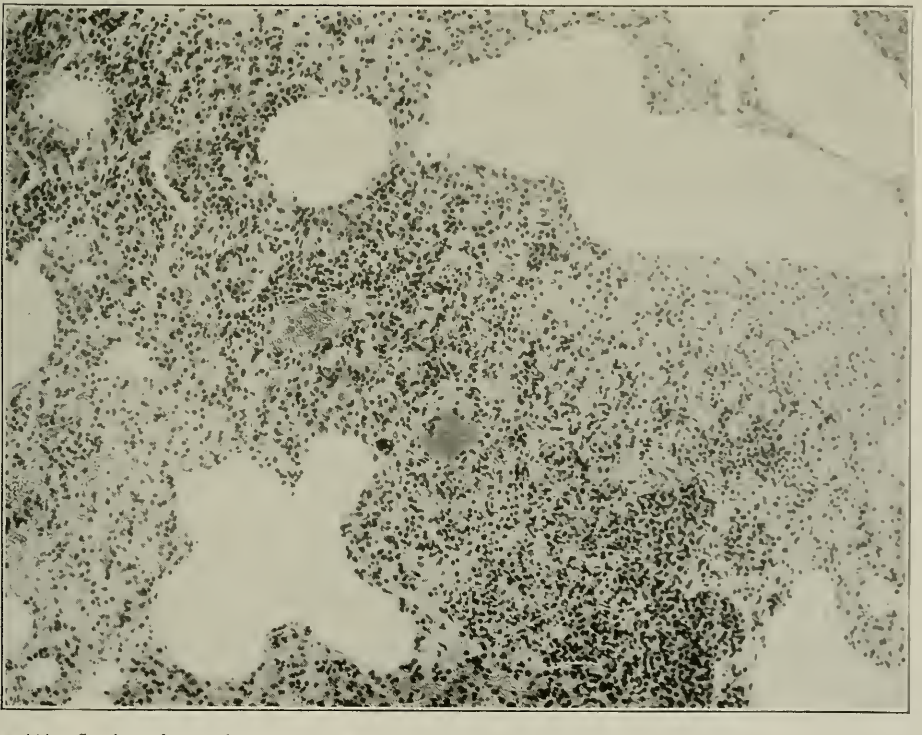

Fig. 111.—Section of lung from same case as preceding. Area of purulent bronchopneumonia with colony of cocci in the center of the field.

membrane, this membrane extending through the nasopharynx and into the larynx and trachea. This membrane was in part firmly adherent to the wall, particularly along the posterior wall, while anteriorly it was loose and separated as a cast of the tracheal tube. Heart showed marked dilatation of both cavities. Pleuræ and pleural cavities negative. Large bronchi filled with purulent exudate. Lungs voluminous, markedly congested and edematous, with the picture of a diffuse bronchopneumonia.

Microscopic Findings.—The microscopic examination of the *nose, nasopharynx, larynx* and *trachea* reveals the presence of a diphtheritic inflammation with a membrane containing numerous colonies of cocci. This membrane is firmly attached wherever the epithelium is completely lost, but is loose and separates from the surface wherever the epithelium is still intact. In the larynx and trachea a large part of the columnar epithelium is replaced by a regenerating layer of large deeply staining pavement or cuboidal cells. The submucosa shows marked congestion, edema, scattered hemorrhages and leucocyte infiltration. The larger *bronchi* are filled with a fibrinopurulent membrane which is adherent to the wall and contains many large colonies of cocci. The epithelium is entirely absent except in a few places where there is a regenerating layer. *Lungs.* The lungs present the picture of an advanced fibrinopurulent bronchopneumonia with large areas of consolidation. All of the bronchioles appear as abscesses. In some of these there are many large epithelial giant cells, syncytial in type, showing an attempt at regeneration, but the great majority show complete destruction of the epithelium. Syncytial epithelial giant cells are also found in some of the alveoli. Colonies of cocci are found everywhere. Many of the pneumonic areas show older and fresh hemorrhages and marked inflammatory edema. (See Figs. 112 to 120.)

This case presents a more marked diphtheritic inflammation of the upper respiratory tract and a diffuse purulent bronchopneumonia due to secondary infection following gassing.

Rabbit 43.—Exposed for twelve hours to a concentration of 1:50,000. Died fifty-four hours after removal from the gassing chamber. In the first stages of the gassing the animal showed nasal irritation, but later became drowsy and depressed, and sat with eyelids nearly closed. At the end of two hours increased lacrimation and conjunctival edema were first noted. When removed from the gassing chamber there was a well marked conjunctivitis with coryza and salivation. The animal would not eat or drink but appeared stupefied. The coryza gradually increased in intensity and within six hours after removal from the chamber bubbling respiratory sounds were heard over its thorax. Coryza and conjunctivitis increased during the first twenty-four hours, at which time there was a profuse seropurulent nasal discharge. The wheezing and bubbling respiratory sounds could be heard some distance from the cage. Respirations were rapid and apparently difficult. Thirty-six hours after gassing the rabbit was still much depressed and the respiratory sounds were louder. The animal frequently sneezed and coughed. There was a marked purulent discharge from the eyes and nose. Forty-eight hours after removal from the gassing chamber the animal was very weak, the respiratory movements more rapid and much forced, the thorax heaving. Both eyes were sealed with a thick purulent exudate. After increasing respiratory difficulty the animal died, fifty-four hours from the time of exposure.

Autopsy.—Marked purulent conjunctivitis with corneal ulceration. Erythema of the exposed portions of the skin. Marked edema of the subcutaneous tissue, particularly in the region of head, neck and thorax. Nose filled with purulent exudate, the mucosa showing deep necroses. Nasopharynx filled with mucopurulent fluid. Larynx and trachea filled with frothy exudate beneath which there was a membranous cast, partly adherent but decreasing in intensity downwards. The mucosa of the entire upper respiratory tract was markedly congested and showed marked necrosis of the surface epithelium. The lungs showed marked congestion and edema. At the base of each lung there was an olive green area, the central portion of which was lighter in color. Bronchi filled with a thick mucopurulent exudate. Pleuræ were negative. Heart showed marked dilatation of the right ventricle. All other organs showed marked congestion. Some cloudy swelling in the kidneys. The external genitals were very erythematous and edematous.

Microscopic Findings.—The *nose* is filled with a diphtheritic fibrinopurulent exudate and the epithelium is completely necrosed, except for very small areas in the folds. The membrane is for the greater part adherent, but loosened in some areas. The submucosa shows marked congestion, leucocyte infiltration, and edema, extending into the muscles and cartilages. The mucosa of the *pharynx* shows a more marked necrosis of the squamous epithelium than in any of the above cases. The cells of the lowest layers are markedly pyknotic. The *larynx* and the *trachea* show a diphtheritic process, the surface being covered with a fibrinopurulent membrane which is firmly attached where the epithelium is entirely absent, but lying loosely on the surface where the epithelium is still intact or regenerating. In the membrane there are colonies of cocci. The epithelium of the larynx and trachea is reduced to a single layer of pyknotic nuclei over a large extent of surface. The submucosa shows marked fibroblastic proliferation, leucocyte infiltration and edema, with minute hemorrhages. The mucous glands of the larynx and trachea show some acini and ducts distended with mucus, but the greater number of the acini appear small, collapsed and pyknotic. The inflammatory infiltration and edema extend into the muscle. The mucosa of the upper part of the *esophagus* shows marked pyknosis and necrosis of the upper layers of the epithelium. The large *bronchi* show a nearly complete necrosis of the epithelium and a fibrinous membrane adherent to the surface forming casts of the bronchial tubes. There is marked congestion of the wall and leucocyte infiltration of the surrounding tissues. The smaller bronchioles are filled with mucous and albuminous exudate with increased leucocytes. The epithelium is intact, but shows mucoid degeneration and pyknosis of the nuclei. A very few bronchi contain a mucopurulent exudate. The *lungs* show extreme congestion, numerous hemorrhages by diapedesis, a few small areas of early bronchopneumonia and atelectatic edematous areas beneath the pleura. The only bacteria found are those in the bronchioles containing the mucopurulent exudate. Marked congestion of all other organs. Cloudy swelling of the liver and kidney cells.

This case differs from the preceding in the severe diphtheritis of the upper respiratory tract with more marked evidences of healing in the larynx and trachea. It shows a severe secondary infective process of the larynx and trachea with less involvement of the bronchi and lungs.

Rabbit 44.—Gassed for twelve hours at a concentration of 1:50,000 at the same time with Rabbit 43. Reaction during the gassing identical. Developed a corresponding conjunctivitis and coryza with similar pulmonary symptoms. This animal, however, survived until 92 hours after the end of the exposure.

Autopsy.—Generalized mustard burn of the skin, especially where the hair was thin, in the form of a marked erythema, marked subcutaneous edema and dilatation of the superficial vessels. The untreated left eye showed a severe purulent conjunctivitis with corneal opacity and superficial ulceration. The right eye had been treated with dichloramine-T and showed a much less severe conjunctivitis and injury to the cornea. The upper respiratory tract was filled with frothy exudate. The mucosa, particularly of the trachea, showed a diphtheritic necrosis with membrane, most marked at the larynx and just below it, but extending into the bifurcation. Bronchi filled with frothy exudate. The lungs were voluminous, with marked congestion and very edematous on section. Atelectatic areas seemed to alternate with emphysematous. At the anterior border of the lowest lobe of the left lung, there was an area greenish gray in color, softened and apparently necrotic. Right ventricle and conus markedly dilated. All other organs congested. In the intestine, small necrotic areas, with inflammatory reaction about them, were found, the entire intestine being markedly congested.

Microscopic Findings.—*Nose.* Slough of the skin of the nose adherent. On the mucous membrane side an ulcer with slough adherent in some areas. Fibroblastic proliferation well developed. *Mouth.* Tongue shows numerous small areas of ulceration and sloughs extending down to the muscle. The remaining portion of the epithelium is intact but shows

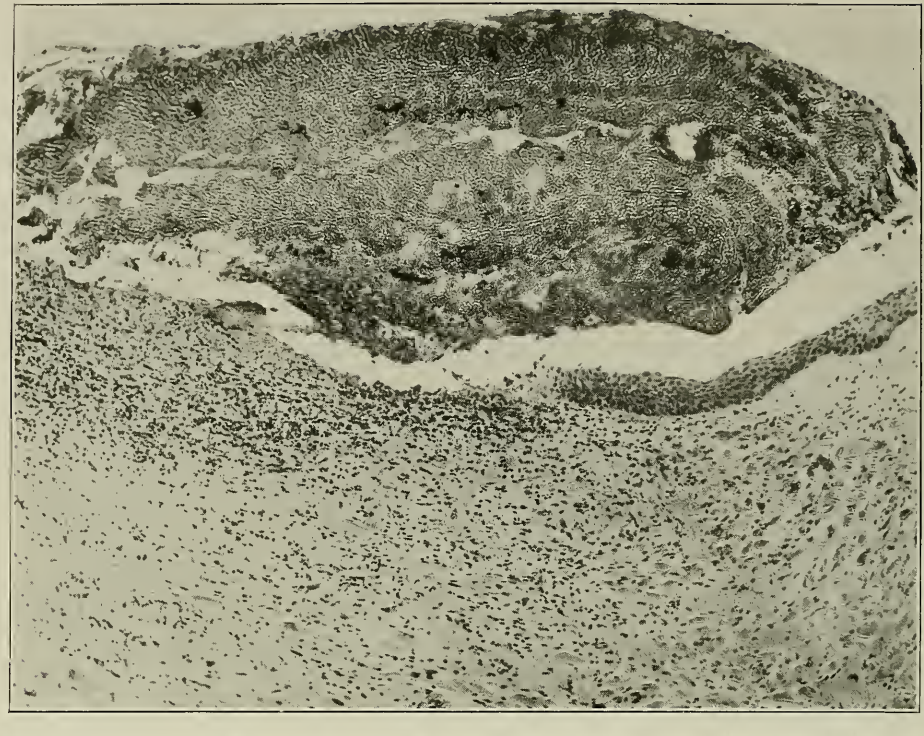

Fig. 112.—Rabbit 45. Exposed for six hours to a concentration of 1:50,000. Died seven days after gassing. Eschar from upper portion of larynx.

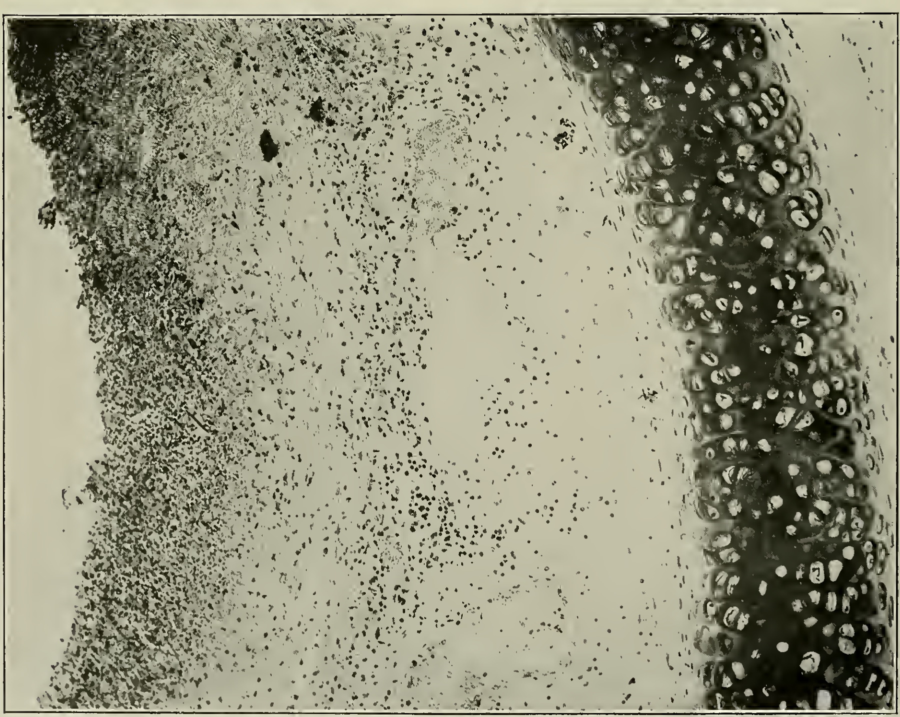

Fig. 113.—Same rabbit as preceding. Section of larynx showing diphtheritic ulcer.

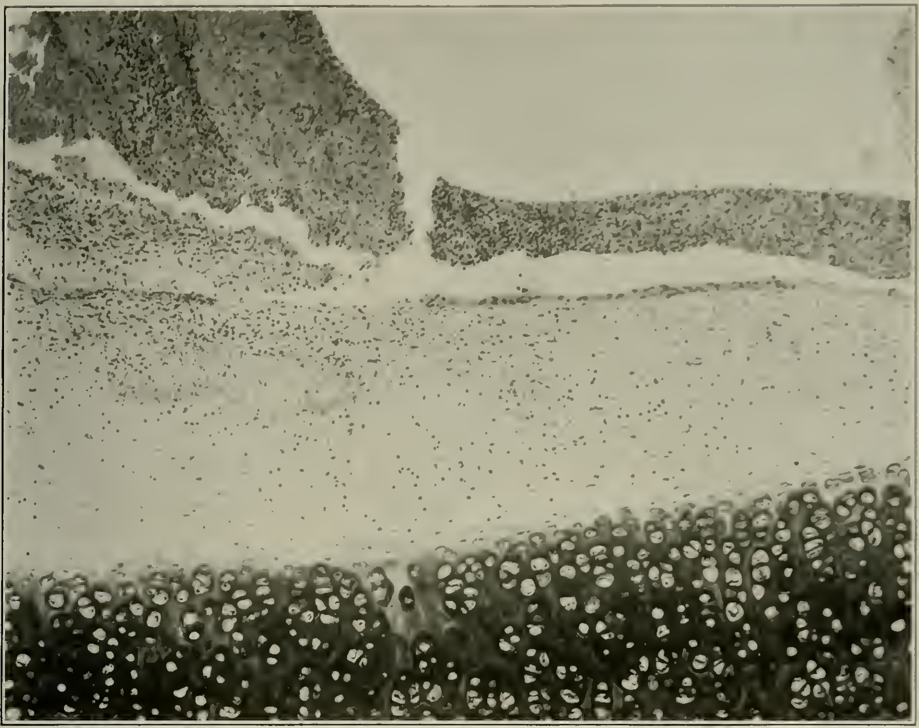

Fig. 114.—Same rabbit as preceding. Section of tracheal wall. Diphtheritic membrane. Epithelium in part gone and in part showing early regeneration. Congestion and edema of submucosa. Small-celled infiltration.

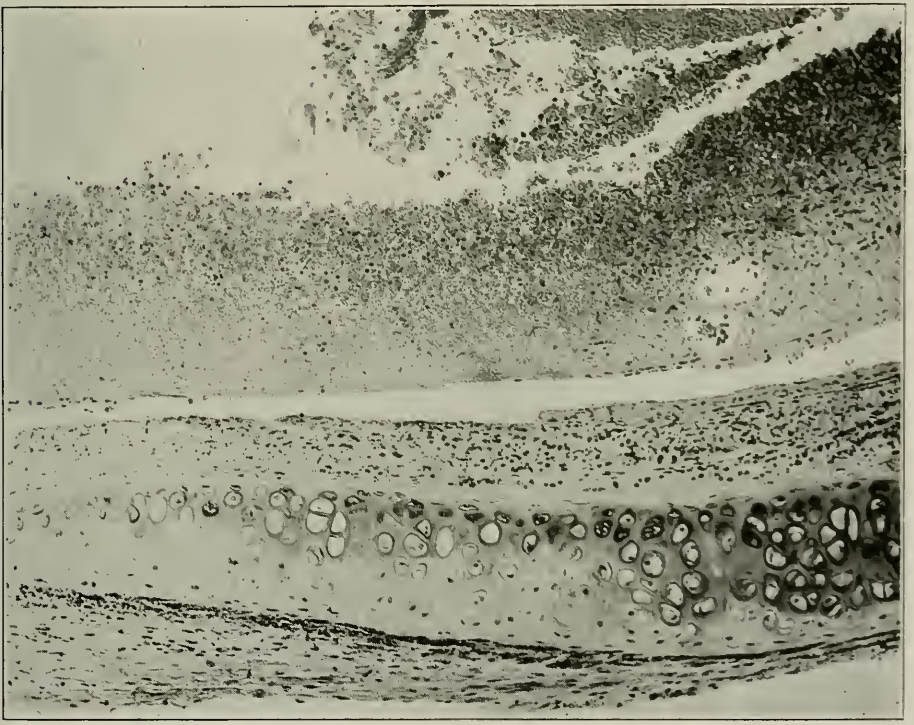

Fig. 115.—Same rabbit as preceding. Wall of large bronchus. Diphtheritic membrane. Complete necrosis of epithelium.

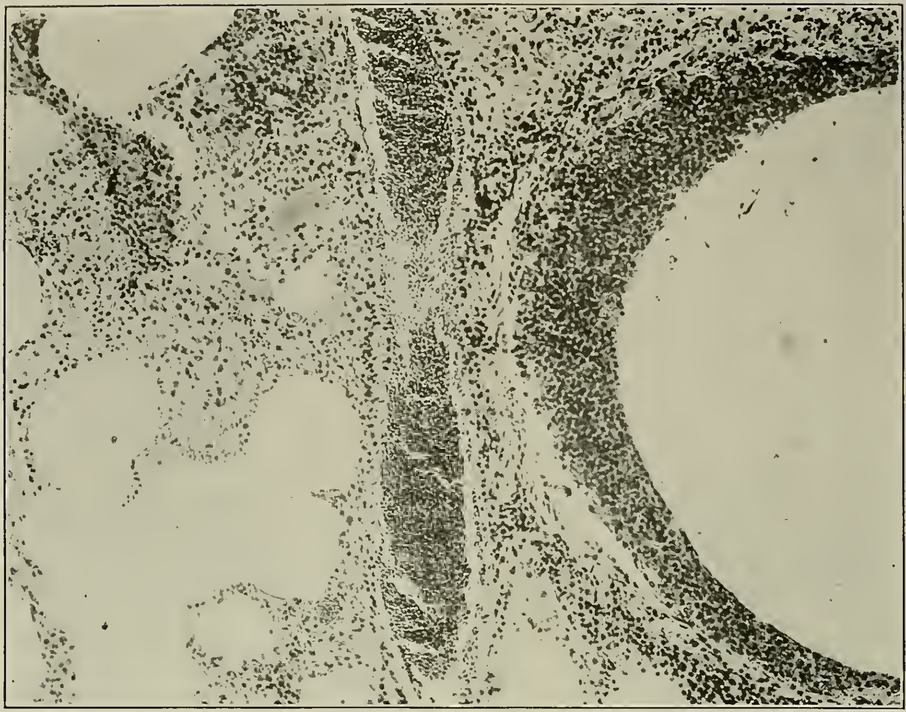

Fig. 116.—Section of medium-sized bronchus from same rabbit as preceding. Complete necrosis of bronchial epithelium; purulent exudate in bronchus. To the left of the congested vessel, colonies of staphylococci in the alveoli.

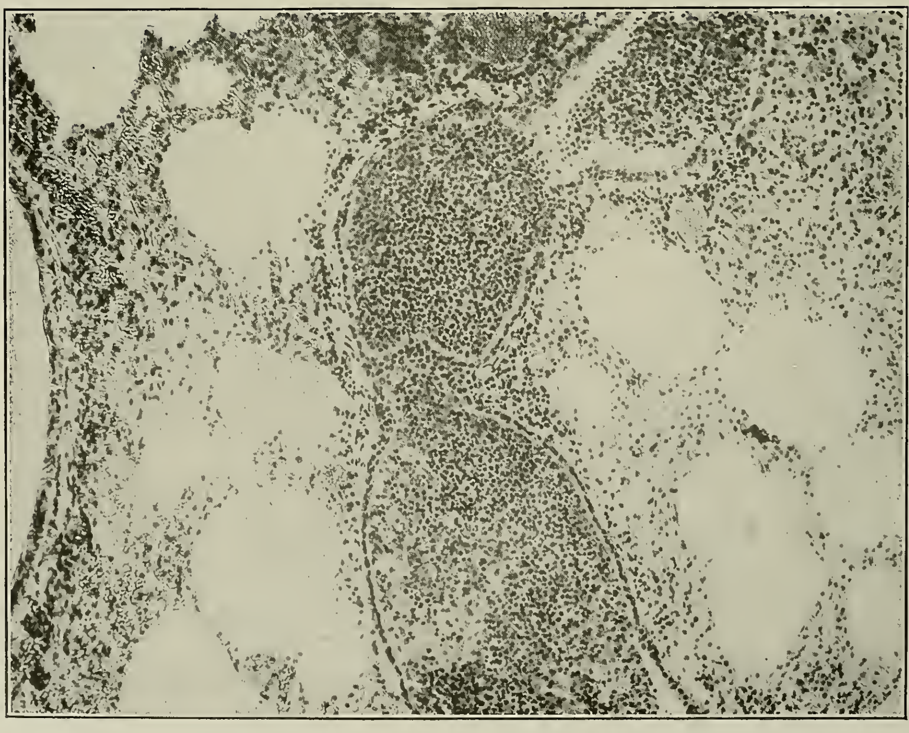

Fig. 117.—Section of lung from same case as preceding. Smaller bronchus filled with purulent exudate.

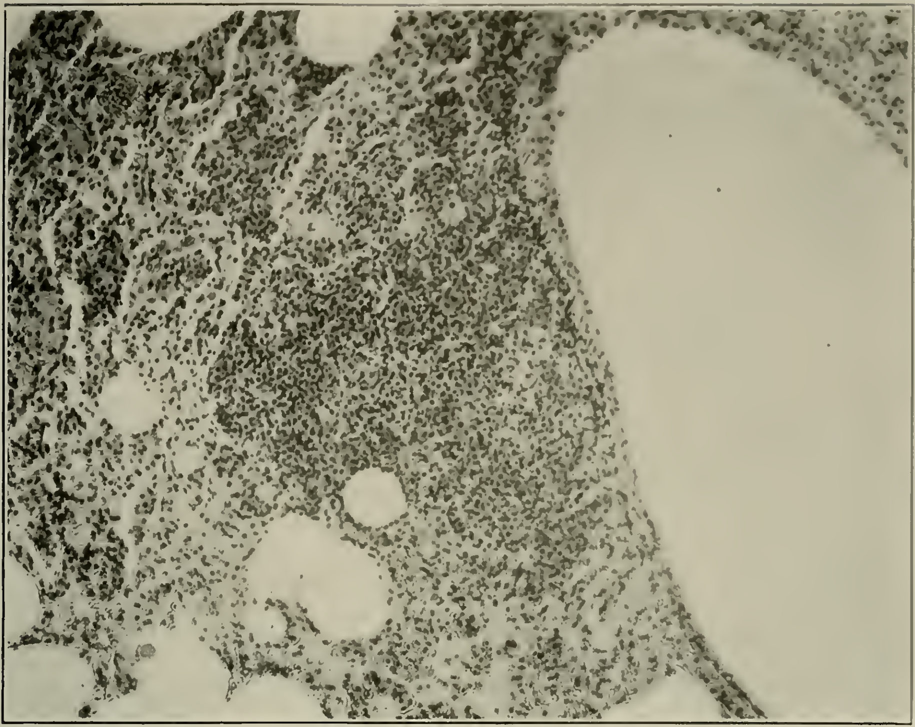

Fig. 118.—Section of lung from same case as preceding. Area of purulent bronchopneumonia with a dilated bronchiole showing necrotic epithelium.

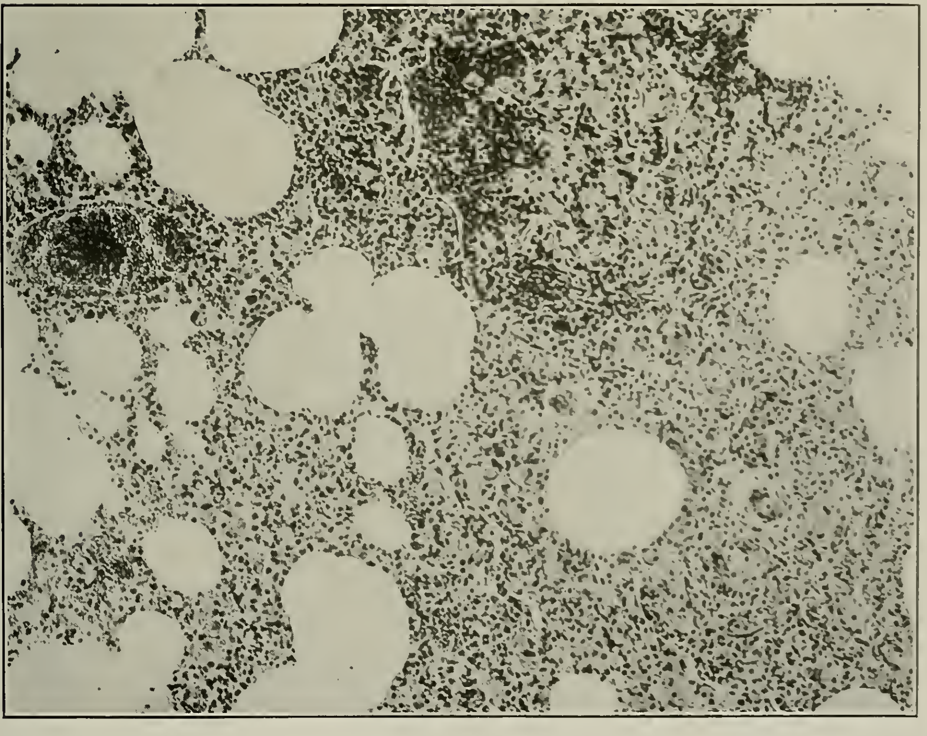

Fig. 119.—Section of lung from same case as preceding. Terminal bronchiole with pus and containing many regenerating epithelial cells. Large syncytial epithelial cells seen also in the neighboring pneumonic area.

pyknosis and contraction of the outer half. *Pharyngeal* mucosa shows the same lesions. Mucous glands of nose and nasopharynx show very marked mucoid degeneration. Intense congestion of the neighboring vessels. Patches of leucocyte infiltration. The *larynx* shows a purulent infiltration of the wall extending to the cartilages. A fibrinopurulent membrane is adherent to the surface over the greater portion and beneath the membrane there is a phlegmonous infiltration of the wall of the larynx. Small patches of epithelium upon the surface have the appearance of regenerating epithelium, regeneration taking place apparently from the ducts of the mucous glands. Numerous colonies of cocci are found in the pus. Below the larynx the epithelium is present over the greater part of the *tracheal* mucosa, which shows mucoid and hydropic degeneration. There are also islands of regenerated epithelium with some fibroblastic proliferation in the submucosa. The tracheal wall shows congestion, edema, small-celled infiltration and fibroblastic proliferation. The larger *bronchi* are filled with pus. Small diphtheritic areas are found on the mucosa, where the epithelium is entirely gone and the fibrinopurulent exudate is adherent. Walls of the bronchi are edematous, infiltrated with leucocytes, and the blood vessels are congested. Any epithelium remaining shows mucoid and hydropic degeneration. The *lungs* show extreme congestion and numerous small hemorrhages. The alveoli for the greater part are overdistended, emphysematous, although there are many small atelectatic areas in the neighborhood of plugged bronchi. The atelectatic areas show a marked edema. Practically all the bronchi and bronchioles are filled with a purulent exudate and around many there are areas of purulent bronchopneumonia. Colonies of cocci are found in the pus in the bronchi. Other organs show intense congestion. No other organs show specific changes with the exception of stomach and intestine, in which small sloughs are found, probably the result of local action of mustard gas swallowed in food or saliva.

This rabbit shows a severe purulent and diphtheritic inflammation of the upper respiratory tract and a purulent bronchopneumonia, due to a staphylococcus, secondary to the more severe lesions caused by the gassing.

Summary of Experimental Work

From repeated and carefully controlled animal experiments we have arrived at the following conclusions in regard to the production and nature of the respiratory lesions due to mustard gassing.

1. The respiratory lesions are proportionate to the concentration of mustard gas employed and to the length of exposure.

2. The mildest lesions are those produced by short exposures, such as ten to fifteen minutes, to dilutions of 1:110,000 or over; or very short exposures, one to several minutes, to higher concentrations.

3. Exposure to mustard gas causes almost immediate signs of nasal irritation on the part of the animal. It will almost immediately rub its nose and turn its back to the inflowing gas. Conjunctival symptoms, in the form of photophobia and increased lacrimation usually appear within two to three hours, the respiratory symptoms developing two to three hours later, as a rule, in the form of snuffles, increased nasal secretion or a more or less severe coryza. In the case of short exposure, or low concentration of the gas, the respiratory symptoms do not progress beyond a catarrhal stage.

4. In prolonged exposures, or exposures to higher concentrations, the respiratory symptoms appear at relatively the same time, but usually later than the conjunctivitis. They then increase in intensity for several days until a picture of diffuse diphtheritic inflammation of the respiratory tract is produced, as manifested by increasing difficulty in respiration, exudation, râles and coughing. The animal may die within forty-eight hours, or later.

5. The pathologic lesions in the mildest cases consist of a superficial degeneration or necrosis of the epithelium of the mucous membrane, with congestion and edema and increased mucus secretion. These milder lesions are found chiefly in the anterior nares, the pharynx, larynx and upper portion of trachea; but animals killed after such exposures invariably show a more or less marked pulmonary congestion and edema, increased bronchial secretion and small, scattered atelectatic areas. From lesions of this degree, recovery, without secondary infection, usually takes place.

6. The severer lesions consist of deeper necrosis of the mucosa of the tract and the formation of a diphtheritic membrane in the anterior nares, nasopharynx, larynx, trachea and larger bronchi. The most severe lesions are always in the nares, pharynx, larynx and upper part of the trachea, the intensity decreasing toward the bronchi. The respiratory columnar epithelium suffers more than the epithelium of the mouth cavity, although irregular areas of complete necrosis of the latter may be produced. The entire epithelium of the larynx, trachea and larger bronchi may be killed outright and the surface covered with a diphtheritic membrane, which, for the greater part, is easily detached, forming a cast of the larynx, trachea and larger bronchi. The laryngeal and tracheal walls show edema, congestion and small-celled infiltration, but the edema is always less marked than in the case of the subcutaneous tissues or the conjunctivæ.

7. In the severe cases, secondary infection with staphylococci almost invariably occurs, and the lesions in the larynx, trachea and bronchi usually take on a purulent character within four to six days, if the animal lives that long.

8. In the mildest cases the lungs show congestion and edema with hydropic and mucoid degeneration of the epithelium of the bronchioles. In the more severe cases the necrosis of the epithelium extends into the smaller bronchial divisions and bronchioles and a secondary purulent bronchopneumonia, apparently usually due to staphylococci, follows. In these severer pulmonary lesions, atelectatic areas, due to the plugging of the bronchioles with exudate, usually alternate with emphysematous areas. The atelectatic areas are usually edematous or hemorrhagic. Secondary hemorrhage into the purulent bronchopneumonic areas is also frequent, in some cases the condition assuming the picture of a hemorrhagic bronchopneumonia. In the pneumonic areas following gassing, colonies of staphylococci are always present.

9. In the severe cases death may occur more quickly as the result of a diphtheritic or purulent laryngitis without the development of pneumonia, but in the majority of cases, the cause of death, so far as the respiratory tract is concerned, is the development of an infective purulent bronchopneumonia secondary to the injury produced by the gassing.

10. Cases with localized diphtheritic necroses in nose, mouth, larynx and trachea, without extensive bronchopneumonia, may recover with healing and cicatrization of these areas. Fibroblastic proliferation in such areas was noted as early as the fourth day after gassing. Cicatricial contractions of trachea or larynx may result from such healed lesions.

Clinical Material

The clinical features of mustard gas lesions of the respiratory tract in man were studied in the cases of seven soldiers who were severely gassed in the manufacture of mustard gas, although wearing gas masks. The concentration of the gas to which these men were exposed was so strong that all received severe burns, two of the cases terminating fatally. In addition to these severe cases, data were secured from 63 other workers with mustard gas who had had at one time or another milder respiratory symptoms following accidental exposure to mustard gas vapor.

Case I.—Private Ha. Exposed one hour in several shifts. Within a few hours after the exposure he developed erythema of the skin, nausea and vomiting and complained of intense thirst. This patient developed no conjunctivitis, his eyes being sufficiently protected by the gas mask. Later, burns about the lips appeared and within the next few days, diphtheritic necroses developed over the dorsum of tongue, uvula, hard and soft palate, pillars of fauces, tonsils and pharynx. On the seventh day after the accident, large moist râles were present over both lungs, and he was thought to have a diffuse bronchopneumonia. The patient died on the eleventh day after gassing. The autopsy report of his respiratory tract changes will be found below.

Case II.—Private S. Exposed three-quarters of an hour, in several shifts, to the same concentration as the preceding. During the next few hours, in addition to the development of conjunctivitis, nausea and vomiting and erythema of the skin, he complained of intense thirst, and later showed patches of diphtheritic necrosis on the lips, angles of mouth, hard and soft palate, uvula, pillars, tonsils, buccal surfaces, dorsum of tongue and gums. All of the mucous membrane of the mouth showed erythema and desquamation of the epithelium. When seen on the eighth day he could barely whisper and had physical signs of a diffuse bronchopneumonia. He died four weeks after the accident. Autopsy not permitted.

Case III.—Private Mc. Exposed forty minutes in four shifts. Within a few hours after the exposure, coincidently with the nausea and vomiting and erythema of the skin, he complained of a very dry throat. For three days he had a hacking cough and complete aphonia. The roof of his mouth was very painful and on the third day one of the sore places in his throat "seemed to burst" and he coughed up membrane-like material, after which his symptoms were improved, but his voice remained husky and a bronchial cough persisted for some time. When examined eight days after the accident he had a catarrhal rhinitis and patches of diphtheritic necrosis over the mucous membrane of the mouth, particularly on the right pillar and in the posterior pharyngeal wall. Occasional loud moist râles were heard over his thorax. Respirations increased.

Case IV.—Private W. Exposed one-half to three-quarters of an hour in two or three shifts. In the first few hours after the exposure he developed mouth and throat symptoms in the form of a dry sore throat and could barely whisper. When examined eight days after the accident he showed diphtheritic necrosis of the mucous membrane of the lips, angles of the mouth, hard and soft palate, uvula, anterior and posterior pillars, tonsils and posterior pharyngeal wall. The roof of the mouth was covered with a grayish green diphtheritic membrane through which numerous discrete yellowish white elevations appeared, suggesting small pustules on erythematous bases. On the eighth day he developed symptoms of a diffuse bronchopneumonia from which he later recovered, after, in the meantime, having expectorated a fibrinous bronchial cast, containing streptococci.

Case V.—Private M. Exposed one-half hour in one shift. Had severe thirst but no soreness of mouth or throat. He developed a temporary erythema of the mucosa of the hard palate with a small patch of diphtheritic necrosis. Voice husky, frequent cough and respiratory rate increased.

Case VI.—Private E. Exposed ten minutes in one exposure. On the next day complained of a very dry throat. He showed only a temporary erythema of the mucous membrane over the hard palate. When seen eight days later his voice was husky, and he had an occasional dry cough.

Case VII.—Private Hu. Exposed ten to twelve minutes in one shift. He developed a severe rhinitis and a sore throat, but showed only an erythema of the mucous membrane of the mouth. When seen eight days after the accident, his voice was still husky, and he had a laryngeal cough.

A large number of other cases of mild respiratory lesions were also seen. All of these were in cases with conjunctivitis. These patients complained usually of a dry or sore throat, huskiness of voice with or without an accompanying rhinitis. A dry laryngeal cough usually persisted for several days, a definite huskiness for a longer period. In two cases, short exposures to weak concentrations produced in susceptible individuals a fibrinopurulent rhinitis lasting several days. In the severe cases of mouth burns the most marked lesions were always on the hard and soft palate and the dorsum of the tongue. The mildest cases showed erythema of the same areas.

Respiratory Lesions as Seen at Autopsy

Case I.—Private Ha.—

Nose.—Examination of anterior nares negative. No skin burns on nose.

Lips.—No burns of mucosa of lips.

Mouth and Neck Organs.—Tip of the tongue is negative. On the dorsum there are patches of grayish and grayish white coating beneath which the mucous membrane is desquamated. When the coating is removed there is a denuded reddened surface. These lesions increase in severity toward the root of the organ where they become diphtheritic in character and are covered with a greenish gray membrane (see Fig. 120). The tonsils and palatal arch show areas of diphtheritic necrosis covered with a grayish membrane. Mucosa of the palate is markedly edematous and presents elevated, reddened and grayish areas. The tonsils are about normal in size, with deep crypts. The right is negative on section. The left tonsil shows membranous patches and, on section, crypts containing fibrinous exudate. Mucosa of pharynx is covered with a thick, grayish, tenacious membrane, which, when pulled off, leaves a denuded, reddened surface. The epiglottis is covered with a thick, grayish mucus and the glottis is filled with a similar mucus. Beneath this the mucosa is congested and shows small patches of superficial necrosis, but these lesions are less marked than in the pharynx. Below the glottis, the mucosa of the trachea is covered with a thick grayish mucus, beneath which the mucosa shows a congestion diminishing in intensity from above downward. There is no membrane in the trachea but in its lower portion and at the bifurcation there is a thick, grayish mucus

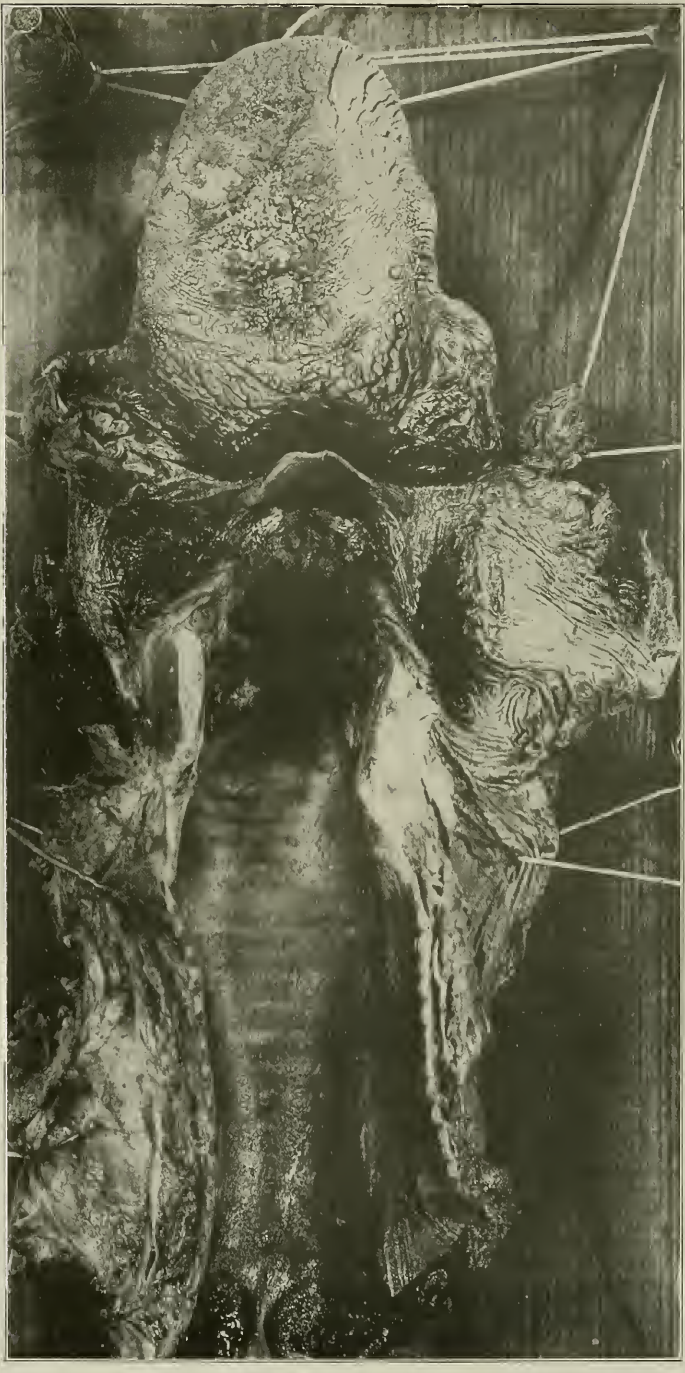

Fig. 120.—Mouth and neck organs of Case I. Mustard gas lesions of tongue, pharynx, larynx, and trachea. Dorsum of the tongue shows diphtheritic eschars. Diphtheritic necrosis of pharynx, mucosa of larynx, and trachea. Marked edema with diphtheritic necrosis of the arytenoepiglottidean fold.

in the lumen. The posterior wall of the trachea shows marked hypostasis but there is no visible necrosis of its mucosa. The esophagus shows congestion of its mucosa with superficial desquamation at the mouth but no changes below this.

Lungs.—There is no fluid in either pleural cavity. The lungs meet in the midline above the heart. Both lungs are free throughout. Pleural surfaces negative.

Left Lung.—There are delicate old adhesions between the upper and lower lobes. On the anterior surface of the lower lobe there is a small pigmented nodule beneath the pleura, a healed tubercle. There is no thickening or puckering of the pleura over the apex. Beneath the pleural surface there are numerous minute petechial hemorrhages which are larger and most abundant posteriorly. The lung is air-containing throughout. The upper lobe is voluminous and pink in color; the lower lobe shows marked hypostasis posteriorly. On section, the cut surface shows marked congestion and edema. Foamy fluid, thicker than the ordinary stasis edema, exudes abundantly from the cut surface. The lower lobe presents a marked hypostatic congestion. The small hemorrhages appear soft and fresh and the blood shows no discoloration. Small fresh agonal lardaceous clots are found in the larger pulmonary vessels, but no thrombi or emboli are visible to the naked eye. No pneumonic areas, no abscesses, no hemorrhagic infarctions and no airless areas are found. Anthracosis is moderate. The main bronchi are filled with a thick, frothy fluid which is rather viscous and is grayish white in color, but in the smaller branches becomes distinctly yellowish and thicker. Beneath this the mucosa of the bronchi is markedly congested.

Right Lung.—The right lung is very much heavier than the left and much deeper in color. There are delicate old adhesions between upper and middle, and middle and lower lobes. The lower lobe posteriorly is almost black in color, the middle lobe deep red, while the upper lobe is more pinkish. The subpleural hemorrhages are more marked in this lung than on the left side. The anterior margins of the lobes show emphysema. The greater part of the lower lobe shows a partial atelectasis and posteriorly a firm airless area almost black in color, about the size of a hen's egg. On section, there is extreme congestion and edema with areas of atelectasis throughout the lower lobe. Throughout the entire lung there are numerous firm, elevated, airless areas of small size, that are not wedge-shaped. The large airless area in the lower lobe is wedge-shaped with its base toward the surface, deep red, almost black in color and shows in its center a softer, lighter area, apparently around the blood vessel. No thrombi or emboli can be seen with the naked eye. The bronchi show the same fluid content and changes in the mucosa as on the left.

Bronchial Nodes.—The bronchial nodes on both sides are rather small, soft, edematous and but slightly pigmented.

Microscopic Findings

Mouth.—Sections from the dorsum of the tongue show patches of diphtheritic necrosis and small ulcers from which the membrane has been loosened. The submucosa shows intense congestion, small-celled infiltration, some fibroblastic proliferation and numerous capillary thromboses. Some of the dilated vessels, either capillaries or lymphatics, are filled with coarse threads of fibrin without red blood cells and with only an occasional leucocyte. The mucous glands show intense mucoid degeneration with small-celled infiltration and many of the ducts are dilated and filled with mucus. Regeneration of the epithelium from the deepest portions of the folds and mouths of the mucous glands has begun. (See Fig. 121.)

Pharynx.—Sections of the pharyngeal wall show intact epithelium covered with a thick mucus. The submucosa shows marked congestion, edema and polynuclear infiltration with small areas of hemorrhage. There are numerous dilated capillaries or lymphatics filled with coarse threads of fibrin without red blood cells or leucocytes. The mucous glands show marked mucoid degeneration. The tonsils show marked congestion and edema. The greater part of the epithelium is intact, but there are localized patches of diphtheritic necrosis. There is an increase of the stroma and many sclerotic vessels.

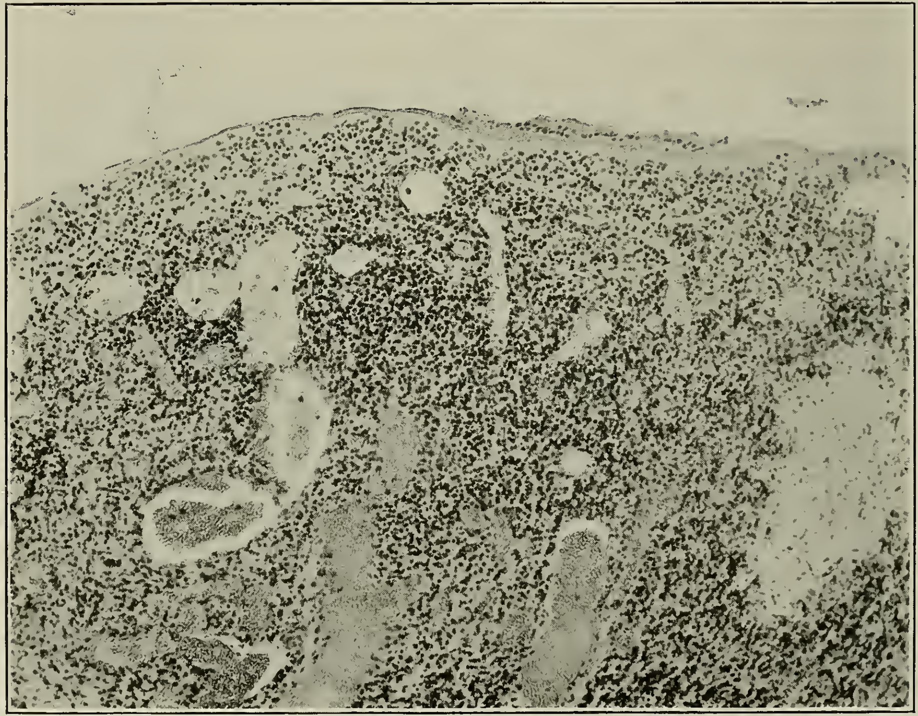

Fig. 121.—Case I, Private IIa. Mustard gas lesion of dorsum of tongue. Base of ulcer from which the diphtheritic membrane has become detached.

Larynx.—Sections from larynx show a desquamative catarrhal laryngitis with small areas of diphtheritis (see Fig. 122). The epithelium is for the greater part necrotic, either entirely gone or represented by a single layer of nuclei. On the surface there is a thick mucofibrinous exudate forming a cast of the entire lumen and for the greater part separated from the necrotic surface. The submucosa shows congestion, edema and slight leucocyte infiltration.

Trachea.—The trachea presents the same condition as the larynx, a desquamative necrotic tracheitis with the formation of a thin mucofibrinous membrane over the surface.

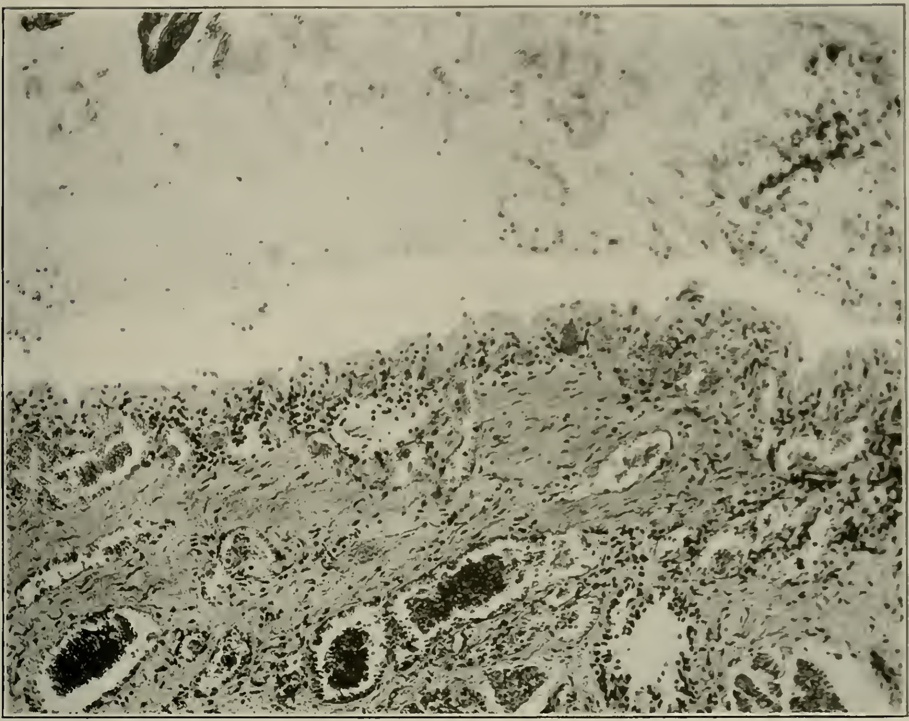

Fig. 122.—Case I, Private IIa. Section of diphtheritic lesion on vocal cord. Epithelium of mucosa completely destroyed and a mucofibrinous membrane partly detached from the surface. Extreme hyperemia of the vessels. Some small-celled infiltration.

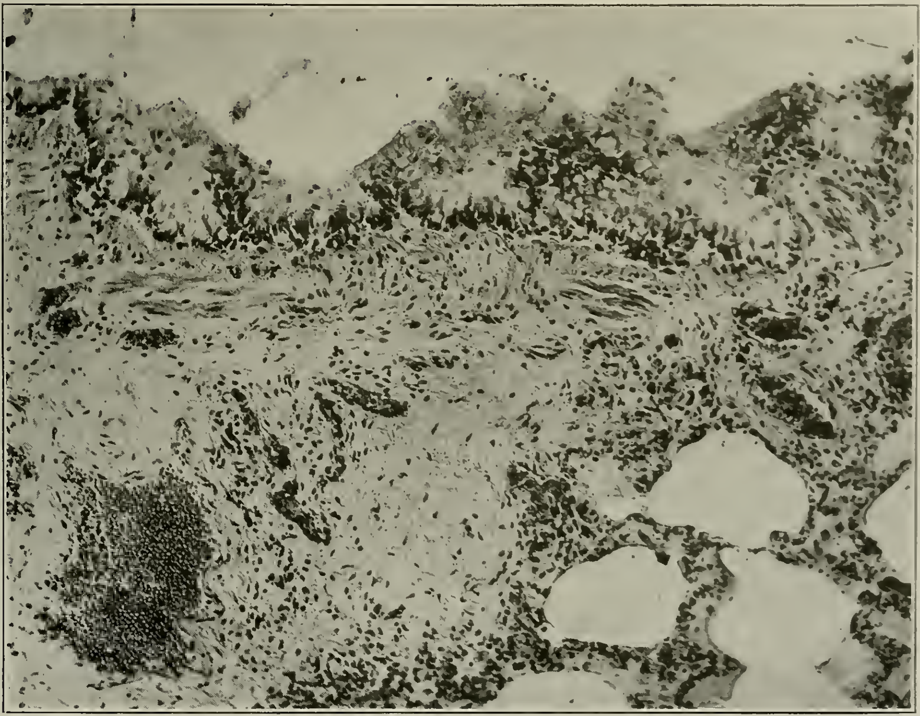

Fig. 123.—Case I, Private IIa. Section of main division of bronchus. Picture of catarrhal bronchitis. Marked mucoid degeneration and vacuolation of the bronchial epithelium. Congestion, small-celled infiltration, and edema of the bronchial wall.

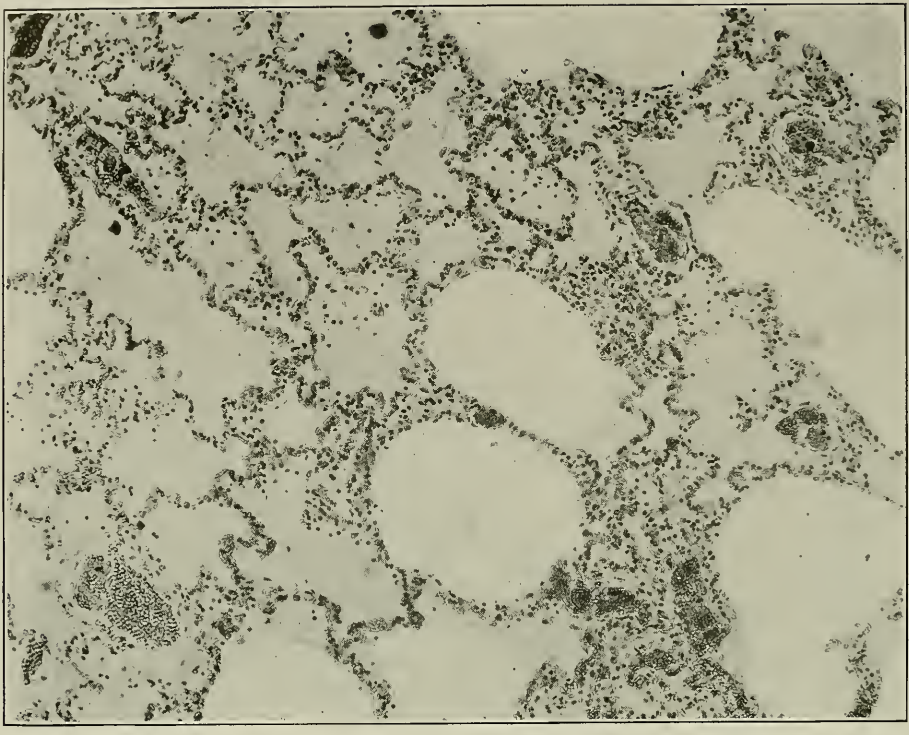

Fig. 124.—Case I, Private Ha. Section from upper lobe of lung. Congestion and edema. Acute emphysema.

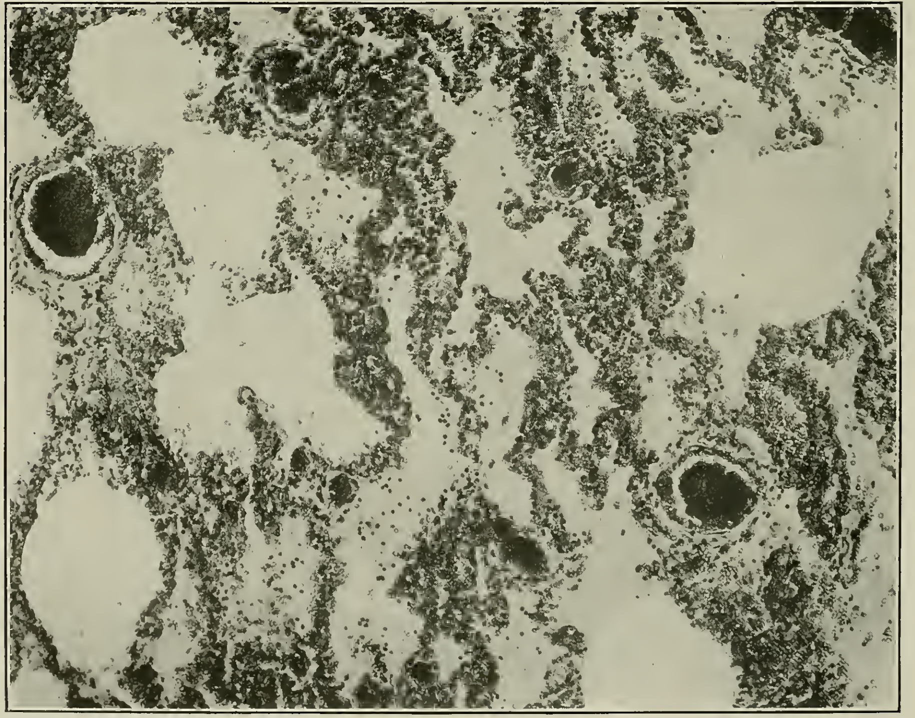

Fig. 125.—Case I, Private Ha. Section of lower lobe of lung. More intense congestion. Minute hemorrhages by diapedesis. Areas of partial atelectasis, alternating with emphysematous areas. Edema.

Bronchi.—The larger bronchi are filled with a thick mucous exudate containing many desquamated cells, some polynuclear leucocytes and a few red blood cells, with little or no fibrin. The epithelium of the mucosa is in part intact, showing hydropic or mucoid degeneration, and in part desquamated. The bronchial walls show intense engorgement of the vessels, well marked edema and a moderate small-celled infiltration. The mucous glands show marked mucoid degeneration. The picture is that of a catarrhal desquamative bronchitis. (See Fig. 123.)

Lungs.—The lungs show extreme congestion and edema with numerous minute hemorrhages by diapedesis. Areas of emphysema and atelectasis alternate throughout the lung. The atelectatic areas show the most marked edema and are usually the areas in which hemorrhages are found. No pneumonic areas are found. The airless area in the lower right lobe is a recent hemorrhagic infarct, the central lighter portion being an artery obturated by a recent mixed thrombus. Other smaller recent hemorrhagic infarcts are found beneath the pleura of the right lung, with recent thrombi in the vessels leading to these areas. All the smaller bronchi and bronchioles are dilated and filled with a seromucoid fluid containing desquamated cells with some fibrin and occasional red cells. The epithelium of the smaller bronchi is intact for the greater part, but shows marked mucoid or hydropic degeneration. In many bronchioles desquamation of the epithelium has taken place. In no bronchi or bronchioles is there any purulent exudate. There are no old thrombi or emboli, and fat stains of frozen sections show no fat emboli. Smears of the bronchial exudate and from the cut surface of the lung show only occasional diplococci. (See Figs. 124, 125.)

This case presents a marked degree of mustard gas degeneration and necrosis of the epithelium of the mouth cavity, larynx and trachea, decreasing in intensity to the larger bronchi and bronchial subdivisions, without infection or pneumonia. Death, in this case, probably resulted from shock and toxemia from the extensive areas of necrosed skin and secondary infection.

Summary of Clinical Observations

From the clinical cases coming under observation, mustard gas lesions of the respiratory tract in man are of the same nature as those produced experimentally in animals. In the milder cases there is an injury to the epithelium of the mucosa of the upper respiratory tract, particularly of the anterior nares, hard and soft palate, dorsum of tongue, pharynx, larynx and upper part of trachea. Rhinitis and laryngeal huskiness and cough with sore throat and thirst are the most common symptoms in individuals exposed to light and moderate concentrations. From these conditions recovery is usually prompt, but laryngeal huskiness and irritation may continue for some days or even weeks. No instances of secondary infection were observed in such cases.

In the more severe human cases, there is a greater degree of degeneration and necrosis of the epithelium of the respiratory tract, extending into the bronchi, but diminishing from the upper part of the trachea down, the most severe lesions being eschars on the palate, dorsum of tongue, pharynx and larynx. Associated with these, there is a widespread catarrhal tracheitis and bronchitis.

with congestion and edema of the lungs. The one case autopsied showed no pneumonia. Under the conditions of warfare more severe exposures to mustard gas may produce diphtheritic lesions of larynx, trachea, and bronchi terminating in bronchopneumonia.

II. Gastrointestinal Lesions Produced by Mustard Gas

Practically no descriptions of gastrointestinal lesions produced by mustard gas exist in the literature. *Giraud* considered lesions of the digestive tract to be rare but thought that they might be caused by ingestion of food contaminated by the gas. In the clinical descriptions given in some of the army medical reports, as in the paper of *Mandel* and *Gibson* (*Journal American Medical Association,* 1917, lxix, 1970-1971), epigastric distress, nausea and vomiting are frequent symptoms and appear in four to sixteen hours after gassing with mustard gas. *Pissarello* (*Giornale di Medicina Militare,* 1918, lxvii, 128-134) states that nausea and salivation are common symptoms in light cases and that vomiting, abdominal pain and diarrhea occur in the severe ones. These symptoms he considers reflex to the coughing. *Canelli* (*Rivista Ospedaliera,* 1918, viii, 2-6) gives the first published report of an autopsy on a case of mustard gas poisoning in which gastrointestinal lesions are described. He found the stomach distended with gas, the mucosa cloudy, glassy, congested in striæ, with numerous minute ulcerations along the major axis. Corresponding to the second flexure of colon there was a small, limited zone of subserous emphysema. The wall of the colon was thick, much congested and the mucosa was everywhere necrotic and covered with a sanious, purulent exudate. Corresponding to the second flexure of the sigmoid the necrosis extended into the submucosa and to the lowest strata of the wall. The duodenum showed a cloudy and congested mucosa, irregularly dotted with minute ulcers on a background similar to that of the stomach. The jejunum and ileum were nearly empty, anemic, semitransparent, with epithelium nearly uniformly desquamated. The esophagus and rectum showed no changes. In his macroscopic pathologic diagnosis, Canelli designates these conditions "acute gastroduodenitis with hemorrhagic erosions; acute desquamative enteritis, similar to the third stage of choleriform enteritis; severe diffuse hemorrhagic necrotic colitis." In his epicrisis he considers the acute inflammation of the colon to resemble macroscopically, in some particulars, both amebic and bacillary dysentery, although not clinically analogous, and considers that the gastrointestinal condition deserves special mention as indicating a selective action of yprite (mustard gas). He states further that in other reported necropsies upon cases dying from the action of other asphyxiating gases, without giving the references, chronic enteritis and gastrointestinal ulceration have been observed, and, therefore, concludes that there is a parallelism between the action of other toxic asphyxiative gases and mustard gas. *Karsner* noted in one autopsy case congestion of the stomach mucosa with submucous petechiæ in the fundus.

Other writers have hinted, without producing pathologic evidence, that the gastrointestinal symptoms are probably the result of mustard gas taken into the alimentary tract on contaminated food; but they may be due in many cases to shock or be secondary to the respiratory conditions.

Experimental

1. Feeding.—Capsules containing .06-.24 c.c. of dichlorethylsulphide were given to rabbits and guinea pigs in olive oil, butter and lard; similar capsules were given in meat to dogs. Animals were kept fasting, but were given water to drink. They were killed in series to get the complete pathologic picture from beginning to end of the process. For the purpose of brevity protocols are omitted, and the results of the experimental work are condensed as follows:

Symptoms.—These appear in 1-12 hours usually. Vomiting; irritation of mucous membranes of mouth; profuse salivation; ultimately foul discharge from nose and mouth; foul diarrhea, at times tarry stools; depression; refusal of food and water. When allowed to live there is progressive anorexia, and weakness; by the sixth day the animals are so weak that they lie prostrate. Animal becomes greatly emaciated, with odor of foul putrefaction. Foul discharge from mouth persists. Death occurs usually by the 12th day, from .03-.06 c.c. doses, within three to five days from the .24 c.c. dose, for dogs; sooner for guinea pigs and rabbits.

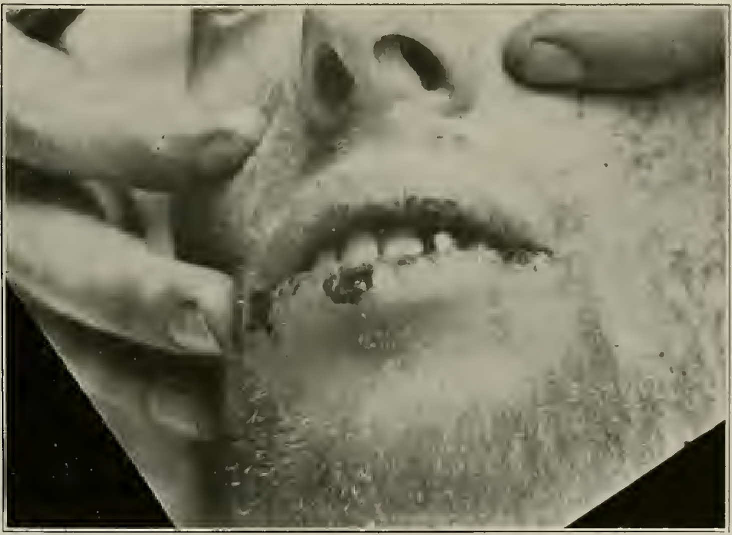

Fig. 126.—Case II, Private S. Mustard gas burns on lip, eight days after exposure.

Gross Pathology.—Delayed rigor mortis in animals not immediately autopsied. Emaciation. No free gas or fluid in peritoneal cavity. No general peritonitis. Liver congested; gall bladder dilated; spleen anemic, small and dry. Heart shows dilatation of right side. Peculiar chicken-fat clots in right ventricle of dogs. Lungs show varying degrees of congestion; no pneumonia. Kidneys congested. Chief lesions in gastrointestinal tract. Stomach and duodenum distended with gas and containing greenish or black fluid. Mucous membrane shows varying degrees of necrosis, localized in patches or extending over the entire surface. The necrosed areas appear greenish brown or gray, to black, without much inflammatory reaction. In the milder cases the mucosa may show marked congestion. Very little hemorrhage in stomach. Necrotic areas are usually thinned, but the animal usually dies before perforation oc-

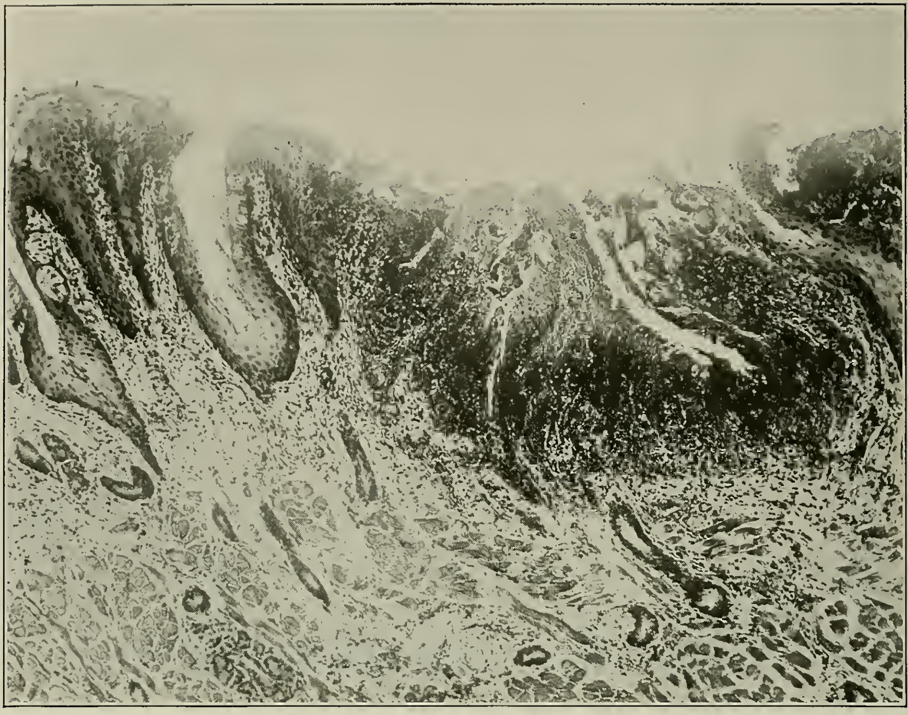

Fig. 127.—Rabbit 44. Exposed twelve hours to a concentration of 1:50,000. Died ninety-two hours after gassing. Mustard gas eschar on tongue.

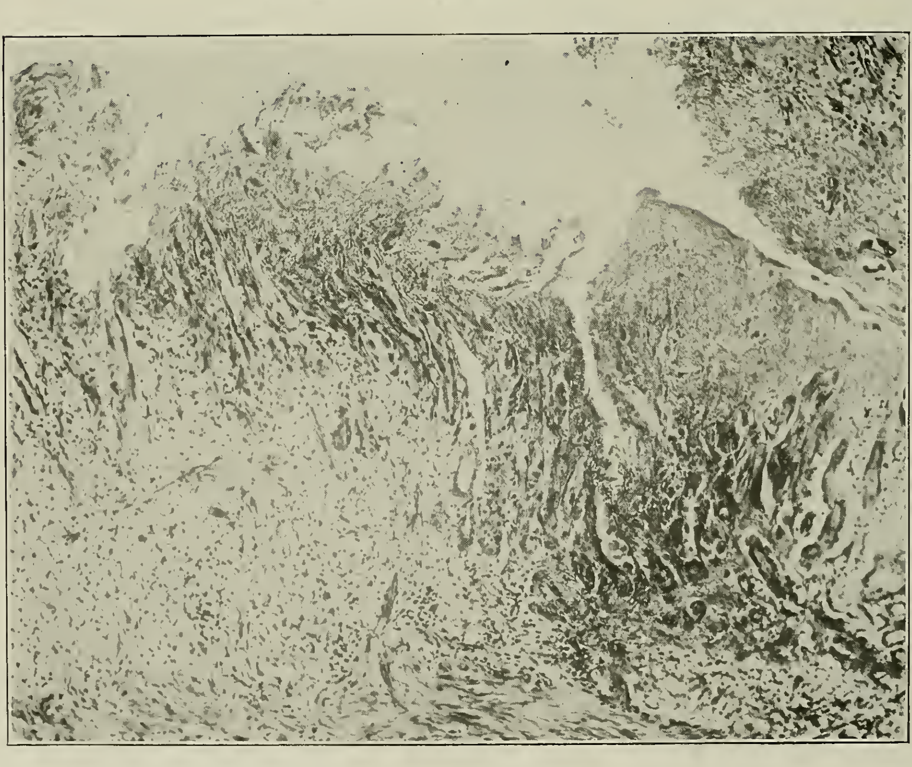

Fig. 128.—Dog. 2. Received four minims of dichlorethylsulphide on meat. Died five days afterwards. Small mustard gas eschar in stomach mucosa. Early fibroblastic proliferation.

curs. Early peritonitis, over the thinned areas, occurs. Self-digestion by the stomach juices of the necrotic surface is delayed, from the inhibition of stomach secretions. Clean ulcers were not seen in the early cases, but were found in from six to twelve days, the ulcer extending into the muscle coat. The stomach lesions do not show the characteristic edema produced by dichlorethylsulphide in the skin and conjunctiva. A moderate edema was observed only in the cardiac end. The nonhemorrhagic character of the gastric lesions is also striking. Throughout the intestines there are patches of necrosis with congestion and slight hemorrhage, and more or less marked catarrh. Mesenteric glands swollen, edematous and congested. In the mouth, nose, pharynx, and esophagus of a certain proportion of the animals marked necrotic lesions, with secondary infection, occurred, as the result of local contact with the gas in swallowing or vomiting.

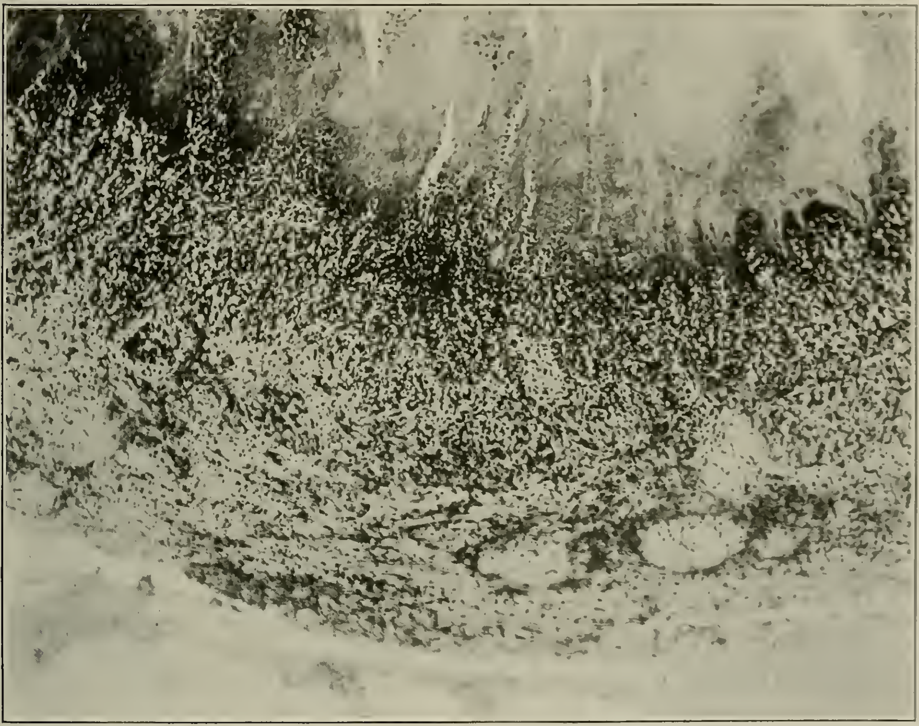

Fig. 129.—Dog 4. Received .06 c.c. of dichlorethylsulphide in capsule. Died twelve days later. Portion of base of very large eschar of stomach wall, extending nearly to the serosa. Marked leucocyte infiltration.

Microscopic Pathology.—Gastrointestinal mucosa shows varying stages and degrees of necrosis, involving the upper layers of the mucosa or extending through the submucosa into the muscle coats. In no case did the ulcer extend through the muscle. Preserved portions of the mucosa show dilated glands filled with granular or thready precipitate, or colloid masses, resembling hyaline casts. The epithelium of the deeper portions of the glands often shows a marked hydropic degeneration or liquefaction necrosis. There is usually little or no edema of the submucosa or tissues of the neighboring stomach wall. The eschar may be adherent to the surface, or the floor of the ulcer may consist of the muscle coats. These show polynuclear infiltration, congestion, some fibrinous exudate into the tissues, and occasionally hemorrhage. In the older cases there is often a marked small-celled infiltration of the muscle coats, extending to the subserosa, with fibroblastic proliferation of the latter and beginning peritonitis. The necrotic areas in the intestine are similar but show a more marked leucocyte infiltration, often extending to the serosa, but without any overlying peritonitis. The necrosis of the mucosa is most marked over the lymphoid tissue; Peyer's patches often being nearly completely necrosed. Numerous putrefactive bacteria are found in the necrotic areas of the mucosa. The entire mucosa is congested, and inflamed, showing occasional hemorrhages. The inflamed mucosa is but moderately edematous. There is marked mucoid degeneration of the epithelium. The mesentery is edematous, and shows at the insertion areas of inflammation. The mesenteric glands show sinus catarrh, and are congested. (See Figs. 128, 129.)

2. Gastrointestinal Lesions in Gassed Animals.—In animals gassed in the gassing chamber and not dying within several days there are found practically always a more or less severe congestion and catarrhal inflammation, which is more severe in the small intestine than in the stomach. In some cases, more severe lesions are found in the upper part of the digestive tract (diphtheritic necrosis, catarrhal inflammation, ulceration, etc.), but these can be explained as the result of gas swallowed with the air, saliva, or with food, and must be interpreted as direct local lesions. (See Fig. 127.) The generalized, catarrhal condition of the small intestine may be explained by the assumption that dichlorethylsulphide or some substance resulting from it is excreted by the intestine or through the bile, or by the direct local action of minute quantities of mustard gas taken in with food or saliva and diffused throughout the gastrointestinal contents.

Clinical Observations

In the severe cases of mustard gassing seen by us, marked nausea and vomiting, gastrointestinal pain and diarrhea either preceded or were synchronous with the development of the cutaneous burns. We believe that these are reflex in nature and can be regarded as symptoms of the severe shock from which the patients suffered at this time. We also believe that the gastrointestinal symptoms seen in several patients after the symptoms of severe shock had disappeared were reflex and dependent upon the laryngotracheal-bronchial irritation (coughing).

In the fatal case the following gross appearances in the gastrointestinal tract were noted:

The *stomach* contains a small amount of thin, grayish fluid, slightly blood stained, and some milk curds. Throughout the entire mucosa there are numerous small petechial hemorrhages, these being most numerous toward the cardia where the mucosa is sprinkled with them, many of them being confluent. They all appear very fresh, the blood not being discolored and no erosions or ulcerations over them. The gastric mucosa is thin, smooth and soft, with early postmortem change. The *duodenum* contains a thin, grayish bile-stained fluid, the mucosa is congested and covered with a tenacious, thick, grayish mucus. Just below the pylorus there are numerous hemorrhages in the mucosa. The *small intestine* is distended with gas and at intervals there are small collections of thin fecal matter slightly bile stained. The mucosa is congested and there is marked hypostasis in portions of the loops without other changes. The *colon* contains gas and some formed fecal masses. The mucosa is negative.

Microscopic Findings.—The *stomach* shows a marked congestion of the vessels of the mucosa with numerous fresh hemorrhages. Postmortem digestion of the upper portion of the mucosa. The *duodenum* shows postmortem necrosis of the upper portion of the mucosa, congestion, and marked mucoid change in the glands of Brunner. The *small intestine* shows a postmortem desquamation of the surface epithelium, slight catarrh of the glands and congestion and edema of the mucosa. *Colon* shows a similar condition. *Appendix* shows evidences of old inflammation. No active process. The *mesenteric glands* show a marked sinus catarrh with many hemophages present in the sinuses.

It is hardly probable that the gastrointestinal changes observed in this case are the direct result of the mustard gassing. It is much more likely that they are entirely secondary phenomena.

(For the gastrointestinal lesions produced by subcutaneous and intravenous injections of mustard gas the reader is referred to the chapter on "The General Pathology of Mustard Gas (Dichlorethylsulphide) Poisoning.")

Conclusions

I. Respiratory Tract

1. The action of dichlorethylsulphide (mustard gas) upon the epithelium of the respiratory tract is escharotic in character, similar to its action upon the epidermis, cornea and conjunctival epithelium. Degeneration or complete necrosis of the epithelium, or deeper necroses extending into the submucosa, constitute the primary lesions produced in the respiratory tract by mustard gas in weak or strong concentrations. These lesions are most marked in the anterior nares, mouth, pharynx, larynx and upper part of trachea, diminishing in intensity toward the lungs. In the more severe cases, however, the bronchial epithelium may also undergo degeneration or necrosis. The subepithelial edema in the upper respiratory tract is not at all comparable in degree to that associated with mustard gas lesions of the skin and conjunctiva.

2. Following the primary lesion there develops a catarrhal or a diphtheritic rhinitis, localized stomatitis, pharyngitis, laryngitis, tracheitis or bronchitis. Cicatricial contractions or sclerosis may result from the healing of such lesions.

3. In even the mildest cases there is marked congestion and edema of the lungs, catarrhal bronchitis and localized atelectasis due to bronchial plugging. In the more severe cases the bronchitis may be diphtheritic in character. Secondary infection may occur, and, following the development of a purulent bronchitis, a purulent bronchopneumonia may result. We have observed no pneumonia resulting directly from the gassing. All of the pneumonias observed, following the gassing, have been the result of secondary infection.

II. Gastrointestinal Tract

1. Direct application of mustard gas to the mucosa of stomach or intestine, by means of contaminated food, produces localized degeneration, necro-

sis and ulceration similar in type to the lesions of the respiratory tract.

2. The mild catarrhal conditions, and small localized eschars of the stomach and upper portion of the small intestine seen in animals gassed in the gassing chamber may be explained as the result of minute quantities of mustard gas swallowed with air or dissolved in the saliva.

3. The gastrointestinal symptoms seen in gassed human beings are probably chiefly reflex, either associated with shock or with the respiratory irritation. As in other forms of gassing, it is probable that erosions or ulcers of the stomach and intestine may be embolic in character, the emboli arising in the primary or infected mustard gas lesions of the skin or elsewhere. It is also possible that in man, as in the case of animals, localized eschars of the gastrointestinal mucosa may be produced by the direct action of mustard gas swallowed in contaminated food or saliva.

NOTE.—Since the above investigation was published, an article on the "Pathology of (Mustard?) Gas Inhalation" by *Covey* and *Barron* has appeared in the Am. Jour. of Med. Sc., 1919, clvii, p. 808. This article gives the gross and microscopic pathology of the respiratory tract lesions in thirty-five cases regarded clinically as mustard gas poisoning. While it does not go into such minute detail, this paper confirms all the important points that we had made in our investigation, and does not add anything essentially new.

Loeper (Le Progrès Médical, March 8, 1919, p. 90) describes a condition of pulmonary sclerosis secondary to mustard gas lesions. We had already pointed out the great probability that chronic bronchitis, peribronchial thickening, bronchial dilatation and pulmonary fibrosis, as well as contractures of the trachea and larynx, would follow the more severe mustard gas lesions of the upper respiratory tract, although at that time we had no personal knowledge of such cases. Since then we have seen returned soldiers showing such chronic lesions, in two cases death occurring two to five months after the gassing. We wish to call attention, therefore, to the fact that the severely gassed soldier presents definite problems as to his future, that are of interest both from the standpoint of pensions and life insurance. We believe that severe gassing must be regarded as a factor lessening the expectancy of life.

CHAPTER V

THE GENERAL PATHOLOGY OF MUSTARD GAS (DICHLORETHYLSULPHIDE) POISONING

Victor Meyer, the discoverer of dichlorethylsulphide, believed that mustard gas applied to the unbroken as well as to the scraped skin of rabbits could produce lesions in other parts not directly touched by the application (eyes and auditory canal). He also made a subcutaneous injection of two drops into the back of a rabbit. No effects were noted at the site of the injection, but the animal developed inflammation of both eyes, with severe snuffles, and died of pneumonia on the third day. From these data he concluded that the most severe action of dichlorethylsulphide develops only after its entrance into the blood. *Haldane* is reported as having confirmed Meyer's observation, by producing conjunctivitis and death from pneumonia through injection. *Kolls and Gilbert* have observed that 10 mg. in an alcoholic solution injected into the muscles and also intravenously caused only a temporary depression and loss of appetite with recovery in a week; but similar injections of 50-100 mg. in alcohol and water emulsion produced convulsions within one hour, and death in three hours.

The general trend of the clinical observations made by French and Italian medical men in field hospitals is to the effect that the lesions of mustard gas poisoning are local, and that no general toxic action is produced. *Giraud* makes the definite statement that all of the lesions observed by him were purely local. He only rarely saw general symptoms, rapid pulse and fever; and these symptoms he thought might be due to other causes than an intoxication. The frequent vomiting he considered dependent upon the respiratory irritation and attempts at coughing. *Mandel and Gibson* do not speak of any general toxic symptoms. *Pissarello* also considered the frequently occurring vomiting to be reflex to coughing. He concluded that ocular symptoms are due entirely to the direct action of mustard gas vapor; and that they are not produced by any substance in the blood of the gassed; and, further, carried out a series of experiments to show that there was no poisonous substance irritant to the conjunctivæ in the tears or sweat of soldiers suffering from mustard gas conjunctivitis. Since gastric symptoms, hemorrhage and ulceration, have been noted in other forms of gassing, notably with chlorine, some writers have assumed their analogous occurrence in mustard gas poisoning.

Canelli, in the first published Italian autopsy protocol of a mustard gas death, notes, in addition to the local lesions of skin and respiratory tract, a parenchymatous degeneration of the liver, fatty cloudy swelling of the kidneys, hemorrhage into adrenal medulla, acute gastroduodenalitis with hemorrhagic erosion, an acute desquamative enteritis, and severe diffuse hemorrhagic necrotic colitis. He seems inclined to the belief that the gastrointestinal lesions are analogous to those produced by other forms of gassing. *Mackenzie* in autopsies upon animals gassed with dichlorethylsulphide observed focal necroses in the liver, punctate hemorrhages in adrenal cortex, swelling and hyperemia of the gastroduodenal mucosa, and in one case hemorrhagic ulcerations near the pylorus. He could not, however, ascribe any positive relationship of these findings to the gassing. *McNee* observed acute hemorrhagic nephritis, degenerative changes in the central portion of liver lobules and minute hemorrhages in the brain, in a few instances. In the four mustard gas autopsies reported by *Karsner* the only pathologic findings, aside from the local lesions of skin and respiratory tract, were a dusky red congestion of all the viscera, including the brain in two cases, and submucous petechiæ in the fundus of the stomach.

The question of the internal pathology of gassing with mustard gas is, therefore, not yet satisfactorily answered; and the object of the investigations recorded in this chapter has been to throw some light upon this problem.

I. General Pathology of Animals Given Local Applications of Dichlorethylsulphide to Skin or Conjunctiva, or Exposed to Its Vapor in Gassing Chamber

From observations made upon a large number of animals exposed to mustard gas, either by direct applications to the skin or eyes, or in the gassing chamber, the systemic symptoms shown consist of gastrointestinal disturbances, such as vomiting and diarrhea; disturbance of heart rate, usually an increased rate, but in severe cases the rate may be slowed; lowering of the temperature except with infection; decreased urinary elimination; in the blood a secondary anemia, with or without leucocytosis; and nervous symptoms, as increased reflex excitability, tremors and convulsions, or marked depression, stupor and coma, The great majority of slightly or moderately gassed animals show no systemic phenomena. The most constant of the general symptoms are the gastrointestinal. While a certain number of cases showing these symptoms may be explained as resulting from slight quantities of mustard gas swallowed in the air or saliva, or on food particles, it is probable that the gastrointestinal symptoms are chiefly reflex to the respiratory irritation, or are a part of the general phenomena of shock. In all severe dichlorethylsulphide gassing an initial shock is very common, and the changes in temperature, circulation, etc., form part of the clinical picture of this condition. With the development of pneumonia or localized infection the usual systemic symptoms attending such processes are observable.

We have seen nothing to make us believe that Victor Meyer's idea, that the toxic action of mustard gas is exerted chiefly through the blood, is correct; indeed, all of our observations make us certain that local applications of mustard gas to the skin of distant parts can not produce conjunctivitis or local lesions at other sites. Meyer's conclusion was based upon an error in technic. The insidious character of mustard gas, the difficulty in handling it, the ease by which invisible droplets, spray or vapor may be conveyed, and the frequent occurrence of such secondary transmitted lesions explainable in this way, are sufficient grounds in explanation of Meyer's incorrect judgment.

Likewise the pathologic findings in gassed animals give no convincing evidence of the absorption of mustard gas into the blood from the skin, eyes, or respiratory tract. The general pathology is as follows:

Central Nervous System.—Congestion; very rarely minute hemorrhages; in infected cases emboli are seen rarely.

Thyroid.—Congestion; no other changes, except as involved directly from the laryngeal lesions. This event is common enough in the severe cases of laryngeal and tracheal diphtheritis, when the thyroid is congested, edematous and infiltrated with leucocytes.

Heart.—Ventricles usually dilated. No changes observable in heart muscle.

Aorta.—Intima of great vessels occasionally shows fatty streaks.

Lung.—When not involved directly through the respiratory tract, as in local application to the skin, the lung shows congestion, with or without edema. In the case of infected skin or eye lesions pulmonary emboli, metastatic pneumonia, etc., may occur.

Spleen.—Congested. In some cases an increase in the number of pigmented phagocytes.

Adrenals.—Congestion. Occasionally minute hemorrhages in medulla. (These are probably postmortem.)

Kidneys.—Congestion. Frequently slight cloudy swelling. In infected cases more marked cloudy swelling, casts.

Pancreas.—Congestion.

Liver.—Marked congestion. In the majority of cases liver cells are normal: slight cloudy swelling and fatty changes are not rare, but their occurrence does not suggest any direct relationship with the gassing.

Gall Bladder.—A thinner, watery bile is usually present.

Gastrointestinal Tract.—Congestion and mucous catarrh are always present. Minute hemorrhages and erosions are frequently seen in stomach (vomiting?). Very rarely embolic hemorrhages and erosions occur, especially in animals with large eschars, or infected lesions. At times local eschars of the gastric mucosa occur; these are explainable as due to ingestion of contaminated food or saliva. The marked salivation seen in many animals and the swallowing of quantities of such saliva containing small amounts of mustard gas, offer a plausible explanation for the catarrhal conditions found in the gastrointestinal tract, without assuming, as some writers have done, that they are due to an excretion of mustard gas through the gastrointestinal mucosa. The intense splanchnic congestion usually present may also serve to explain the gastrointestinal conditions.

Mesenteric Lymph Nodes.—Congestion and edema.

Genital Organs.—No changes noted.

Urinary Bladder.—Negative.

II. General Pathology as Shown in Human Autopsy

The protocol of the gross and microscopic general pathology of the one human autopsy case of fatal poisoning from mustard gas seen by us is given here in full, with the exception of the respiratory and gastrointestinal tracts, which are given in the preceding chapter.

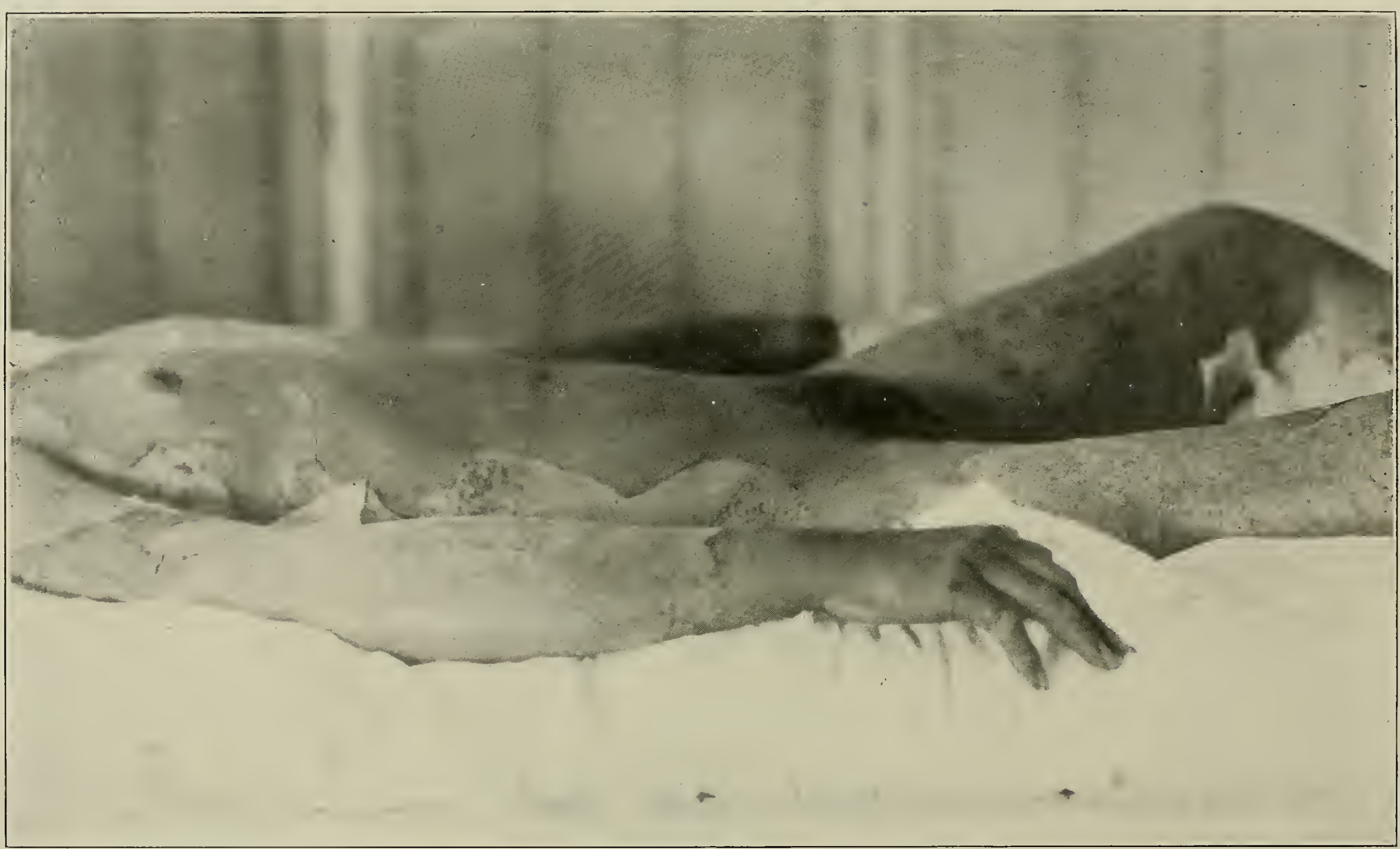

Fig. 130.—Fatal case of mustard gas poisoning. Death on the eleventh day after one hour's exposure to a strong concentration of dichlorethylsulphide vapor.

AUTOPSY PROTOCOL.—*Private Ha.* Died 12:30 A.M., July 8, 1918.

(Autopsy by Dr. A. S. Warthin, 2:00 P.M., July 8, 1918.)

External Examination.—Young adult male body, length 170 cm., strong build, frame large, thorax deep, epigastric angle a right angle, abdomen on level with ribs. Musculature good, well developed. Panniculus abundant, particularly over abdomen and thighs. Hips rounded, slightly of feminine type. Neck thick, thyroid small, facies slightly suggestive of mouth breathing; general appearances of body suggest the lymphatic constitution. All regional lymph nodes prominent. Hair of head abundant, dull brownish in color, dry; scalp shows much dandruff. Face shaven, beard not heavy, body hair fairly abundant, pubic hair of feminine type. External genitals small, scrotum small, tight; testicles small; penis medium size, moderate phimosis. No anomalies. No deformities, defects or mutilations. No surgical wounds or scars.

Hypostasis.—Moderate postmortem hypostasis, pale in color, except over hyperemic areas. Superficial veins on upper portion of body contain but little blood.

Rigor Mortis.—Marked rigor mortis throughout body, except in right arm, where it has been broken by manipulation of the arm.

Body Heat.—Body is cold. (Cooled by undertaker.)

Odor.—Marked odor of gangrene over the skin, particularly from that of back.

Skin.—Marked pigmentation of skin of face, hands and forearms. Right hand shows irregular patches of pigmentation alternating with paler recent scars of older (mustard gas) burns. Hands show irregular patches, particularly between the fingers, of desquamation of the horny layer. No recent burns on hands.

Over the greater part of the body, from the collar line down to the boot line, the skin presents the appearance of a chemical burn, varying in degree from hyperemia, slight desquamation, dried blebs and bullæ, denuded areas, to areas of well-marked necrosis and eschar formation. These lesions are most severe in the axillary regions, inner aspect of arms, bends of elbows, flanks, genitals, thighs and back. Severe lesions completely encircle both thighs, particularly marked posteriorly where there is extreme necrosis, secondary infection and pus formation. The necrosis is very marked over the entire back, neck, shoulders and buttocks, where the skin is discolored, mottled red, grayish, yellowish gray, brown, black or greenish, with marked gangrenous odor. Deeper points of hyperemia corresponding to the hair follicles show in these discolored areas. Over a large part of these lesions the epidermis is desquamated in large bullæ, and the desquamated surface is brown, yellow or red. There are no large hemorrhages into these lesions, and very few petechial hemorrhages, the reddened areas being hyperemic only, the redness disappearing on pressure. From the discolored moist areas a cloudy foul-smelling serum exudes. This is not blood stained in any region. Through the hyperemic areas in many regions the hair follicles appear as opaque, yellowish miliary nodules. These are particularly marked over the scrotum.

The skin of the abdomen is hyperemic with a pale belted line corresponding to the protection afforded by belt worn by patient. This belted area of less injury disappears in the flanks and shows but slightly on the back. The anterior surfaces of the thighs are bright scarlet, marked hyperemia. The hyperemia stops rather abruptly over the legs about 15 cm. below the lower border of the patella. The lower portions of the legs show practically no involvement anteriorly; posteriorly there is slight discoloration and hyperemia (hypostasis?). The feet show no lesions.

The *face* shows no lesions except on the right side, around and below the right ear, where there is a slight desquamation of the epidermis, with some reddening of the edges and elevated portions of the lobe of the ear. Below the left ear there is slight desquamation without reddening. Over the *neck*, below the chin, are patches of dried vesicles, brownish red where the epidermis is desquamated, and red where it is still intact. The *hair* shows no changes. On the *scalp* the only lesion found is an area of hyperemia above the right mastoid prominence. Here the scalp is scaly with a large amount of dandruff.

It is notable that the skin over the bony prominences, particularly over clavicles, scapulæ, etc., shows circumscribed patches of deeper eschar formation.

The areolæ of both nipples show strikingly the greater intensity of the injury around the hair follicles and sebaceous glands. Each nipple is surrounded by a deep zone of hyperemia in which the epidermis has been lost; through the hyperemic skin the yellowish, enlarged hair follicles can be seen.

The skin of *penis* and *scrotum* is discolored, necrotic and gives off a foul gangrenous odor. There is a well-marked phimosis, but the small portion of the glans exposed, around the meatus, is necrotic, yellowish and infiltrated with pus. A drop of pus exudes from the meatus. The remaining portion of the mucosa of the glans shows a marked inflammatory reaction (hyperemia, infiltration and edema). Through the discolored skin of the *scrotum* the yellowish necrotic enlarged hair follicles and sebaceous glands stand out prominently. Around the anus there is a zone of marked gangrene and suppuration of the skin.

The areas of skin (face, hands, legs and feet) not affected by the lesions show marked anemia.

Mucous Membranes.—These are pale, particularly the lips. They are dry but show no burns. Tip of the tongue shows no lesions. (See below.)

Eyes.—The cornea and conjunctivæ of both eyes are clear; there is no hyperemia, no discharge, no opacity. No signs at all of conjunctival involvement.

Nose.—Nasal openings negative.

Ears.—Auditory passages negative.

Edema.—Trace only about ankles; none in eyelids or below eyes. Over the burned areas the skin is swollen, tumefied, infiltrated, consistency increased, but pits only slightly on pressure.

MAIN SECTION

On section the panniculus is abundant, pale yellow, moist shining, and only slightly edematous. The superficial veins are markedly anemic. No free gas in *peritoneal cavity.* Abdominal recti deep red in color, with lighter patches of hyaline or Zenker's necrosis (as in typhoid.) *Omentum* lies a handbreadth below the umbilicus, is very rich in fat; its vessels are empty.

There is no free fluid in the cavity. The *peritoneal surface* is clear, shining, rather dry, but shows no signs of inflammation. Upper coils of *small intestine* are distended with gas. *Cecum* is greatly distended, also *transverse colon,* and *descending colon* as far as the sigmoid.

Hepatic and *splenic* flexures collapsed.

Stomach in normal position, contains a small amount of fluid and gas. Vessels of stomach enormously congested. Pylorus is in normal position. Old adhesions around the *appendix,* but no active process. The appendix is 10 cm. long, patent throughout, and empty.

Lower border of *liver* in median line is three fingerbreadths below the ensiform, and about one fingerbreadth below costal margin in the right nipple line. The *spleen* is in normal position, the lower pole about two fingers above the costal margin.

The *diaphragm* on the left is in the 5th i.c.s., and at the 5th rib on the right.

The *thoracic muscles* are deep red, very dry and anemic.

The *costal cartilages* are white, and cut easily.

No free gas or fluid in the *pleural cavities.*

The *sternum* shows normal consistence, and its red marrow is in normal amount and appearance.

The *anterior mediastinal fat* is very abundant and shows numerous petechial hemorrhages. The fat is very abundant over the *pericardial sac,* and shows numerous petechial hemorrhages.

The *thymic fat* is abundant and contains numerous petechial hemorrhages. In it, the *thymus* is still present in the form of two distinct lobes, each of which is 5 cm. long and 3-5 mm. thick. Its color is pink, consistence firm; no hemorrhages in its substance.

The *lungs* meet in the middle line above the heart. The *apex* of the heart is in the 5th i.c.s., inside the left nipple line.

Both *lungs* are free throughout. There is no fluid in either pleural cavity.

Pericardium.—No gas in pericardial sac; fluid normal in amount, clear amber. Pericardial lining smooth, clear, moist, shining.

Heart.—Heart is small, smaller than cadaver's right fist; in marked rigor mortis, the left ventricle completely contracted, and the right one nearly so. The *auricles* and *venæ cavæ* are collapsed, nearly empty; on section contain but a small amount of dark fluid blood. The subepicardial fat is in excess; over the pulmonary artery, just above the conus, is a sclerotic patch ("soldier's spot") about the size of a dime; along the coronary branches, posteriorly over the left ventricle, are narrow stripes of sclerosis. There are numerous subepicardial hemorrhages, most marked in the neighborhood of the auriculoventricular groove. On section the heart contains a very little fluid blood and small thin lardaceous agonal clots, particularly in the right ventricle, extending into the pulmonary artery.

The *mitral* opening admits two fingers; the flaps are negative. In the left auricle a small agonal lardaceous clot. The left ventricle wall measures 20 mm. in thickness, the *muscle* is deep brownish red, firm, and shows no cloudiness, fibroid patches or fatty change. No fatty change seen beneath the endocardium.

The *tricuspid* opening admits three fingers barely. Its flaps are normal. Small agonal clot in right auricle. The *foramen ovale* is patent, an oval slit admitting probe 3 mm. in diameter, but well guarded by membranous curtain. The *pulmonary artery* admits two fingers, the pulmonary semilunar valves are negative. The *right ventricle* wall measures 3-8 mm. in thickness, about one-half of this being fat tissue. The *aortic opening* admits the thumb easily. Its semilunar flaps negative. The beginning of the aorta shows very fine stripes and patches of fatty degeneration of the intima. Arch of aorta negative; also its main branches. Pulmonary artery and main branches empty and negative.

(For protocol of lungs, see chapter on Respiratory Lesions.)

Examination of *thoracic duct* negative.

Thoracic aorta shows linear stripes of fatty degeneration.

(For protocol of mouth and neck organs, see chapter on Respiratory Lesions.)

The cervical *esophagus* shows some injection of its mucosa at its mouth with superficial desquamation; below this no changes except postmortem hypostasis. A small amount of stomach contents in the lower portion.

The *thyroid* is small; but on section shows normal amount of colloid.

Parathyroids, four in number, brownish in color, about normal size.

Cervical nodes are about normal in size, some larger, translucent, slightly edematous.

Parotid and submaxillary glands are normal in size and appearances.

Great vessels and nerves of neck region are negative.

Abdominal Organs.—The *spleen* is somewhat enlarged, soft, flattens on the board, its capsule slightly wrinkled. On its surface are the remains of a few old adhesions to the diaphragm. On section the pulp is soft, deep brownish red, rises above the trabeculæ, the cut surface slightly shagreened. Bleeds rather poorly. Follicles barely visible. There are no infarcts, abscesses, or other lesions apparent.

The *adrenals* are surrounded by abundant fat tissue. Both are normal in size, the cortex pale yellow and somewhat fatty, the medullary portions showing no postmortem changes. No pathologic changes apparent.

The *kidneys* have large fatty capsules. Fibrous capsules strip very easily. Both kidneys somewhat enlarged, plump and markedly congested. Surfaces smooth, veins congested. On section both kidneys bleed freely. The cut surface shows extreme congestion: the outlines between labyrinths and medullary rays are not distinct. The surface is slightly cloudy (slight or moderate cloudy swelling). The pelvis of the left kidney is negative: that of right is dilated, filled with cloudy urine, and its mucosa slightly injected.

The left *ureter* is normal in size and appearance; the right is dilated with cloudy urine.

The *urinary bladder* is moderately distended, containing about 60 to 70 c.c. of turbid urine. Mucosa is pale, negative.

The *prostate* is of normal size and shape; on section normal in appearance.

The *seminal vesicles* contain a small amount of thin brownish semen on the right side; on the left they are nearly empty; and the walls show some thickening.

The *testes* show congested tunics. No fluid in sacs. On section both organs are rather small, slightly congested and slightly edematous. The left testis shows slight fibrosis extending from the rete.

(For protocol on gastrointestinal lesions see preceding chapter.)

The *liver* is much enlarged, particularly the right lobe; but the lower border is rather sharp. Capsule negative. Surface smooth. Color deep brownish red with paler anemic areas. On section bleeds very freely. Consistency fairly firm. Cut surface uniform deep reddish brown, the lobules enlarged, with congested central areas and slightly cloudy parenchyma (slight cloudy swelling). Anemic areas show slight fatty shine.

The *bile passages* are patent. Gall bladder small, contains a moderate amount of thick brownish bile, no concretions.

The *portal vein, common duct* and *inferior vena cava* negative on section.

The entire *splanchnic area* is congested.

The *retroperitoneal* and *mesenteric* lymph nodes are enlarged, markedly congested and somewhat edematous. The prevertebral *hemolymph nodes* are hyperplastic, deep red, and very numerous.

The *thoracic* and *abdominal aorta* small in size (hypoplastic), empty; the intima shows linear stripes of fatty degeneration, most marked in the neighborhood of the celiac axis.

Semilunar ganglia and *solar plexus* negative.

NERVOUS SYSTEM.—*Head.*—The *scalp* is negative except for changes mentioned above. Periosteum of cranium negative. In the right parietal bone a circular area of slight hyperostosis resulting from a cephalhematoma at birth. Corresponding to this area of elevation, there is on the inner surface of the *skull cap* a marked pacchionian depression almost perforating the greatly thinned outer table. The skull cap is thin; dura adherent all over; the meningeal grooves and pacchionian depressions unusually marked for age of cadaver; the lamina vitrea rough and dull; the dura is thickened throughout. The arachnoid shows numerous focal thickenings; the subarachnoid fluid is markedly increased (edema); no evidences of inflammation. *Central longitudinal sinus* is negative. The *basal meninges* are slightly thickened and unusually tough.

The *basal vessels* are negative.

The entire *leptomeninges* are somewhat thickened, but strip easily.

The *cerebral convolutions* are rather sharp, but show no focal lesions. The ventricles are somewhat dilated; the cerebrospinal fluid is increased greatly, but is clear. The *ependyma* is normal.

The *chorioid plexus* is markedly congested on both sides. The *pineal* gland is normal in size and appearance. On section the *cerebrum* shows congestion and edema. No hemorrhages found.

The *cerebellum* shows marked congestion and edema. Dentate nuclei are normal. No lesions in cerebellar lobes. The *basal ganglia, internal* and *external capsules* are negative.

The *pons* and *medulla* are congested and edematous. No lesions apparent.

The *cervical cord* shows slight congestion and edema. No lesions seen.

The *hypophysis* is of normal size, congested.

Basal sinuses congested. Base of skull negative.

PROVISIONAL GROSS PATHOLOGIC DIAGNOSIS.—"Mustard gas" burns of skin and upper respiratory tract; gangrene and secondary infection of skin; shock; toxemia; edema, congestion and early hemorrhagic bronchopneumonia. Passive congestion of all organs. Splanchnic congestion marked. Moderate parenchymatous degeneration of kidneys and liver (toxic); multiple petechial hemorrhages; congestion and edema of brain and cord; thymicolymphatic constitution.

MICROSCOPIC FINDINGS

Cerebrum.—Sections taken from all parts of the cerebral cortex, basal ganglia, floor of ventricles, internal capsule, show intense congestion, edema and a few minute perivascular hemorrhages.

Pons, Medulla and *Cerebellum.*—Show a similar congestion and edema.

Meninges.—Old thickenings. No active process. Marked congestion of the vessels and edema. In the larger pial veins there are agonal clots rich in leucocytes.

Hypophysis.—Intense congestion, otherwise negative.

Pineal Gland.—Large calcareous concretion. Gland substance smaller in amount than normal. Marked edema.

Spinal Cord.—Edema. Congestion. Postmortem myelinosis.

Heart.—Subepicardial fat abundant. Vessels congested. Numerous petechial hemorrhages throughout the fat. Heart muscle fibers somewhat smaller than normal—an acute simple atrophy. Stroma somewhat increased around the coronaries in the left ventricle wall. Endocardium is negative. Heart muscle shows very slight parenchymatous degeneration. No fat. Mixed agonal clots taken from the heart show white clot with very few leucocytes while in the red portions of the clot there are large collections of leucocytes.

Aorta.—Stripes of marked fatty degeneration in the intima. These are longitudinal and stain rather brownish red with sudan III and also a brownish red with scarlet red. Osmic acid not successful.

(For respiratory tract and neck organs, see preceding chapter.)

Thyroid.—Vessels congested. Otherwise negative.

Cervical Lymph Nodes.—Show marked sinus catarrh with numerous hemophages in the sinuses. The *cervical hemolymph nodes* show marked congestion and hemolysis, many hemophages in the sinuses.

Thymus.—Remains of thymus scattered throughout the thymic fat with large corpuscles of Hassall, many of which are calcified.

Spleen.—Marked acute passive congestion. Small hemorrhages scattered throughout the pulp. Acute lymphoid exhaustion. Follicles very small with central exhaustion. No degeneration of the central portion of the follicles seen as in burns of the skin. No thrombi, no emboli or infarcts.

Adrenals.—Slight cloudy swelling of the cortex. No increase in fat content. Congestion. Edema. Chromaffinic substance small in amount.

Kidneys.—Intense congestion. Cloudy swelling, particularly of the convoluted tubules. Numerous small precipitates of phosphates in the straight tubules of the cortex (concentrated urine). Marked edema of the connective tissue around the larger vessels and of the medullary portion. Very few casts. Frozen sections show no fat.

Bladder.—Congestion and edema. Otherwise negative.

Prostate.—Congestion. Gland spaces filled with secretion and desquamated epithelium. No pathologic changes. The prostatic plexus contains an organizing thrombus.

Seminal Vesicles.—Negative. The one apparently hyaline, shows only collapse of the wall; empty but no fibrosis.

Posterior Urethra.—Negative.

Testes.—Very little normal spermatogenesis. Many atypical division figures and desquamation of spermatids. Stroma is increased throughout, basement membrane thickened. Appearances suggest an old mumps orchitis. Intense congestion of the vessels.

Epididymes.—Negative.

Penis.—Foreskin edematous. Vessels congested, with areas of complete necrosis of the epithelium and of the subepithelial tissues. Where the epidermis is intact the horny layer is thickened and the epithelium beneath shows evidences of regeneration. The glans shows likewise areas of necrotic epithelium with areas of regeneration and other patches in which the horny layer is greatly thickened and adherent. The meatus shows a slight inflammation. The body of the penis shows areas of regenerating epithelium covered with a dense desquamated horny layer. Large areas of the surface are denuded, the epithelium necrotic, the necrosis extending into the subepithelial tissues. Marked congestion and edema throughout the organ and a mild diffuse inflammation.

Liver.—Acute passive congestion. Slight cloudy swelling. Fat stains show no fatty degeneration but a few scattered cells containing large droplets of fat.

Pancreas.—Congestion. Early postmortem softening. No other pathologic changes. Islands numerous, many of them very large.

Stomach.—Postmortem digestion of upper part of mucosa. Congestion. Hemorrhages.

Duodenum.—Postmortem necrosis of mucosa. Marked mucoid change in glands of Brunner.

Small Intestine.—Postmortem desquamation of epithelium. Congestion. Edema. Slight catarrh.

Colon.—Similar changes.

Appendix.—Evidences of old inflammation. No active process.

Mesenteric Glands.—Lymphoid hyperplasia, with exhaustion of the germ centers. Marked sinus catarrh. Many hemophages.

Retroperitoneal Hemolymph Nodes.—Marked congestion of sinuses. Great numbers of hemophages.

Skin.—The skin taken from various portions of the body shows complete necrosis of the epidermis and greater part of the corium reaching as far as the sweat glands over the greater part of the surface, but in many instances reaching the subcutaneous tissues. Many colonies of bacteria are found upon the necrotic corium but there is very little leucocytic infiltration in the necrotic corium or at the border between the living and dead tissues. Only in scattered areas where there is evidently a localized secondary infection are there any notable collections of polynuclears. The vessels in the lower portion of the corium show intense congestion, stasis. In the lymphatics there is a heavy albuminous precipitate with coarse fibrin threads. The lower border of the corium and upper portion of the subcutaneous fat shows usually a well-marked edema. No old thrombi are found and very few hemorrhages, only here and there have a few red blood cells escaped from the vessels. More recent clots with heavy threads of fibrin are found in many of the distended vessels. In these clots many hemolyzed red blood cells are seen. Some hyaline clots are found in the areas of marked necrosis and secondary infection, but these may be secondary to the latter process. Fibroblastic proliferation has begun at the lower border of the necrotic corium and is particularly marked around many of the blood vessels and sweat glands. Regeneration of epithelium from the hair follicles and sweat glands has begun in many areas and in some instances extends to the surface. Separation of the eschar has begun in some areas. Every degree of change is shown from areas where the necrotic epithelium is still adherent, to those areas where the slough is beginning to separate, and to areas of beginning regeneration. A striking feature of the process is that the sebaceous glands are everywhere completely destroyed, but islands of regenerating squamous epithelium mark the site of these glands. The sweat glands also show marked degeneration, the majority of the acini being necrotic or hydropic. Regeneration of epithelium occurs almost entirely from the hair follicles and ducts of the sweat glands. Around the nipple, in the axillary region and over the scrotum the necrosis is deeper and more marked and the large sweat glands of the axilla show marked degeneration. In the scrotum the necrosis extends deep into the dartos involving the superficial bundles of involuntary muscle. In the scrotum, also, regeneration of epithelium proceeds from the hair follicles.

FINAL PATHOLOGIC DIAGNOSIS.—Mustard gas burns of skin and upper respiratory tract. Necrosis, secondary infection and gangrene of skin. Acute necrotic pharyngitis. Acute catarrhal laryngitis, tracheitis and bronchitis. Congestion and edema of lungs. Multiple hemorrhagic infarctions of lungs. Acute passive congestion of all organs. Multiple petechial hemorrhages. Marked fatty degeneration of intima of aorta. Parenchymatous degeneration of kidneys and liver. Splanchnic congestion. Shock. Toxemia. Secondary anemia. Hypoplasia of heart and aorta. Thymicolymphatic constitution. Hyperplasia of hemolymph nodes with excessive hemolysis. Organizing thrombus in prostatic plexus. Old orchitis (mumps?).

SUMMARY OF CASE

The pathologic findings in this autopsy case give no evidence of a systemic action of dichlorethylsulphide. All of the changes seen can be explained as due to the direct local action of the mustard gas vapor, or as secondary to the shock and secondary infection of the lesions.

III. General Pathology Resulting from Subcutaneous and Intravenous Injections of Dichlorethylsulphide

Series of animals, rabbits and dogs, were given varying amounts of dichlorethylsulphide by subcutaneous and intravenous injection. Two samples of very pure dichlorethylsulphide were used, one furnished by Major Moses Gomberg, and the other by the Chemical Warfare Service. For the subcutaneous injections in rabbits, a site on the right side of the back was constantly employed. The hair was clipped or shaved over an area six centimeters in diameter and the liquid dichlorethylsulphide was injected into the subcutaneous fascia above the spinal muscles. In dogs, also, the injection was made beneath the skin of the back. For the intravenous injections in rabbits, the superficial femoral and jugular veins were used. The pure substance was used, instead of oily solutions, because of the great danger of fatty embolism with the latter. In most cases, the animals were allowed to die, but some were killed in order to avoid postmortem change in the tissues. In all cases, autopsies were done, the tissues were fixed in formol, and sections of all organs were stained in hematoxylin and eosin, and other routine stains.

(A) SUBCUTANEOUS INJECTION OF DICHLORETHYLSULPHIDE

The following condensed protocols are selected as representative of the reactions following injection of varying amounts of dichlorethylsulphide. Rectal temperatures, daily weights and character of feces are given, and these, taken together, serve to indicate the severity of the reaction.

RABBIT 55.—Subcutaneous injection of .015 c.c. of dichlorethylsulphide. Very slight general reaction, with apparently complete recovery, except for the local lesion, twenty-six days after injection.

DATE		TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec.	16	102.3°	1870	.015 c.c. dichlorethylsulphide subcutaneously.
"	17	102.5	1750	No diarrhea.
"	18	102.7	1740	" "
"	19	102.6	1870	" "
"	20	103.1	1880	" "
"	21	102.6	1930	" "
"	22	102.6	1950	Slight diarrhea.
"	23	103.2	2010	No diarrhea.
"	24	103.5	1970	" "
"	25	102.6	2010	" "
"	26	102.6	2060	" "
"	27	103.0	2100	" "
"	28	103.3	2200	" "
"	29	104.1	2090	" "
"	30	103.4	2200	" "
"	31	103.1	2130	" "
Jan.	1	102.8	2120	" "
"	2	103.3	2070	" "
"	3	103.0	2140	" "
"	4	102.6	2150	" "
"	5	103.3	2130	" "
"	6	102.8	2090	" "
"	7	103.0	2090	" "
"	8	103.4	2090	" "
"	9	103.5	2150	" "
"	10	102.2	2300	" "
"	11	102.8	2190	No diarrhea. Lesion is now nearly healed. There is a hairless area about 1 cm. in diameter, which is covered with a shiny smooth cicatrix except for a small area in its central portion.

Rabbit 48.—Subcutaneous injection of .03 c.c. of dichlorethylsulphide. Slight general reaction. Living, thirty-seven days after injection, with apparent complete recovery, except for the local lesion.

DATE		TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec.	5	101.6°	2100	.03 c.c. dichlorethylsulphide subcutaneously. No signs of local irritation.
"	6	102.6	2020	No diarrhea. Animal very thirsty.
"	7	102.0	2050	" "
"	8	103.0	2060	" "
"	9	101.0	1990	" "
"	10	101.8	1940	Slight diarrhea.
"	11	103.6	1950	No evidence of diarrhea.
"	12	102.4	1990	Perianal hair somewhat soiled.
"	13	103.6	1900	No diarrhea.
"	14	104.4	1870	" "
"	15	103.9	2000	" "
"	16	103.2	2030	" "
"	17	102.7	1930	" "
"	18	102.6	1830	" "
"	19	101.6	1810	" "
"	20	102.6	2040	" "
"	21	103.6	2000	" "
"	22	102.2	2080	" "
"	23	102.1	2110	" "
"	24	102.7	2090	" "
"	25	103.3	2000	" "
"	26	101.6	2060	" "
"	27	102.0	2070	" "
"	28	102.3	2150	" "
"	29	103.5	2110	" "
"	30	103.7	2140	" "
"	31	103.6	2170	" "
Jan.	1	103.1	2020	" "
"	2	102.9	2030	" "
"	3	102.8	2250	" "
"	4	103.5	2170	" "
"	5	103.2	2060	" "
"	6	103.4	2020	" "
"	7	103.2	1990	" "
"	8	102.1	2020	" "
"	9	102.6	2060	" "
"	10	102.8	2240	" "
"	11	102.6	2100	No diarrhea. The local lesion is not yet completely healed. There is an indurated area about 1 by 1.5 cm. over which there is an incomplete regeneration of epithelium. This area is firmly adherent to the underlying tissue.

Rabbit 47.—Subcutaneous injection of .03 c.c. of dichlorethylsulphide. Moderately severe reaction. Death on the twelfth day. Protocol by days in table on opposite page.

Autopsy

Autopsy at 1:45 P. M. Body warm. No rigor. *Pleural cavities* and *pleuræ* negative. *Heart* contracted. The right auricle still pulsates when stimulated. The *lungs* show a

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 5	102.5°	1520	.03 c.c. dichlorethylsulphide subcutaneously. No evidence of local reaction.
" 6	102.8	1430	No diarrhea.
" 7	102.1	1490	No diarrhea. Edematous area at site of injection measures 2 by 6 cm.
" 8	101.8	1460	No diarrhea.
" 9, 9:30 A.M.	97.6	1380	" "
" 9, 10:30 P.M.	97.0		Hair soiled about anus and soft fecal material on thermometer.
" 10, 9:30 A.M.	98.6	1250	Diarrhea.
" 10, 5:00 P.M.	96.0		"
" 11, 9:00 A.M.	99.0	1120	"
" 11, 5:00 P.M.	96.7		"
" 12, 9:30 A.M.	99.8	1155	"
" 12, 4:30 P.M.	100.2		Hair soiled, but feces formed.
" 13	101.6	1100	No diarrhea.
" 14	101.5	1060	" "
" 15	100.8	1060	" "
" 16	101.7	1070	" "
" 17	97.2	995	Appears much sicker. Perianal hair soiled, but no diarrhea noted.
" 17, 1:00 P.M.			Died.

moderate congestion with hypostatic areas posteriorly in the lower lobes. The *liver* is congested, otherwise negative. The *gall bladder* is not distended. The spleen shows a moderate congestion, likewise the *kidneys*, in which there are also some edema and slight cloudy swelling. The *stomach* is nearly empty and the mucosa shows no changes. The upper small *intestines* are slightly edematous. Formed stools are found in the *colon*. No evidence of diarrhea. At the root of the mesentery there is a lobulated mass of edematous hyperplastic lymph nodes.

MICROSCOPIC FINDINGS.—*Lungs.* Slight congestion. No edema. *Heart.* Negative. *Spleen.* Congestion. In the sinuses are great numbers of pigmented hemophages, the pigment varying in color from brown to almost black. Hemosiderosis. *Kidneys.* Moderate congestion. Very slight cloudy swelling. Practically negative. *Adrenals.* Negative. *Stomach.* Negative. *Small Intestine.* Congestion and edema of mucous membrane with necrosis of the superficial epithelium of the tops of the folds and villi. Glands of Lieberkühn show excessive mucus formation and individual glands show necrosis. Minute erosions occur along the mucosa. The *liver* shows marked passive congestion, a nutmeg liver with acute central necrosis in many lobules. The bile ducts show an unusual mucous degeneration of the epithelium with edema of the surrounding connective tissue. There is a complete necrosis of the epithelium of the *gall bladder* and of its basement membrane. The neighboring liver tissue also shows a zone of necrosis as from the diffusion of some necrosing substance from the gall bladder. At the *site of injection* there is a large area of necrosis extending through the striped muscle into the fascia. About this, there is a zone of fibroblastic proliferation and leucocyte infiltration. The striped muscle in the neighborhood shows a marked Zenker's necrosis.

RABBIT 50.—Subcutaneous injection of .06 c.c. of dichlorethylsulphide. Moderately severe reaction. Apparent recovery, except for local lesion. Animal killed on the 32nd day after injection. Protocol by days in table on page 178.

AUTOPSY

Pleuræ, pleural cavities, heart and *lungs* are negative. The *stomach* is distended with food; its mucosa appears negative. The *gall bladder* is small: the bile, pale. *Liver.* Congestion. *Spleen.* Congestion. *Kidneys.* Slight cloudy swelling and congestion. The upper small *intestines* contain a small quantity of thin fluid material. There are no formed

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 6	101.7°	2020	.06 c.c. dichlorethylsulphide subcutaneously.
" 7	101.8	2000	No diarrhea. Very thirsty.
" 8	101.6	2130	No diarrhea.
" 9	100.0	2060	" "
" 10, 9:30 A.M.	100.9	1990	" "
" 10, 5:00 P.M.	98.6		Perianal hair somewhat soiled.
" 11, 9:00 A.M.	100.0	1920	Diarrhea.
" 11, 5:00 P.M.	98.6		Marked foul diarrhea.
" 12, 9:30 A.M.	99.6	1840	Diarrhea.
" 12, 4:30 P.M.	101.7		Perianal hair still soiled.
" 13	102.6	1790	" " " "
" 14	102.6	1840	Stool slightly soft.
" 15	102.4	1820	" " "
" 16	102.7	1840	Perianal region still somewhat soiled.
" 17	101.8	1710	No diarrhea.
" 18	102.0	1650	" "
" 19	102.3	1640	" "
" 20	102.2	1740	No diarrhea. Quite weak.
" 21	103.0	1710	" "
" 22	101.8	1660	No diarrhea. Weak and appears very sick.
" 23	102.9	1680	No diarrhea. Appears stronger.
" 24	103.0	1650	" "
" 25	103.2	1680	" "
" 26	102.6	1740	" "
" 27	104.0	1780	" "
' 28	102.7	1800	" "
" 29	102.9	1810	" "
" 30	103.9	1910	" "
" 31	103.6	1950	" "
Jan. 1	103.6	1900	" "
" 2	103.4	1870	" "
" 3	102.9	1910	" "
" 4	103.2	2030	" "
" 5	102.9	1940	" "
" 6	102.7	1930	" "
" 7	102.9	1970	No diarrhea. The local lesion now measures 15 by 30 mm. It is dry, nonpurulent and shows slowly progressing healing.
" 7, 2:30 P.M.			Animal killed. Autopsy at once.

stools in the colon, but no evidence of diarrhea. The intestinal mucosa shows no lesions to the naked eye.

MICROSCOPIC FINDINGS.—*Heart.* Negative. *Lungs.* Congestion without edema. Small patches of bronchopneumonia. *Spleen.* Marked congestion with a fairly large number of pigmented phagocytes. *Kidneys* and *adrenals.* Negative. *Stomach.* Negative. Mucosa well preserved. *Liver.* Congestion. Slight cloudy swelling. Bile ducts negative. *Gall bladder.* Epithelium well preserved. No necrosis. *Intestine.* Marked catarrhal enteritis. Epithelium well preserved. No desquamation. Lumen nearly empty. *Pancreas.* Congestion. *Mesenteric lymph nodes.* Extreme edema.

RABBIT 63.—Subcutaneous injection of .06 c.c. of dichlorethylsulphide. Severe reaction. Animal killed on the fifteenth day. Protocol by days in table on opposite page.

AUTOPSY

Pleural cavities, pleuræ, heart and *lungs* negative, except for numerous firm, slightly caseous areas at root of right lung, probably an old tuberculosis. *Peritoneal* cavity contains about 50 c.c. of clear fluid. *Liver.* Congestion. *Gall bladder.* Moderately distended

DATE	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 23	105.0°	2810	.06 c.c. dichlorethylsulphide in deep subcutaneous and intramuscular injection.
" 24	103.6	2770	No diarrhea.
" 25	103.0	2580	" "
" 26	102.0	2610	Slight diarrhea.
" 27	102.1	2580	Diarrhea.
" 28	99.7	2500	"
" 29	98.5	2450	Marked diarrhea.
" 30	100.9	2260	" "
" 31	101.6	2120	" "
Jan. 1	101.8	2130	Diarrhea.
" 2	103.0	2050	Stools formed but moist. Marked edema of right half of abdominal wall.
" 3	102.9	2060	No diarrhea.
" 4	103.4	2100	" "
" 5	103.1	1950	" "
" 6	102.0	1920	" "
" 7	100.5	1840	" "
" 7, 1:30 P.M.			Killed. Autopsy at once.

with thin bile. *Stomach.* Moderately filled. No visible lesions of the mucosa. *Intestines.* Peristalsis very active. Thin mucoid fluid in upper small intestine. In the cecal pouch there is much thick gruel-like fecal material with denser oval masses adherent to the mucosa. Formed stools in colon. *Kidneys.* Congestion and slight cloudy swelling. *Adrenals.* Congestion. *Mesenteric nodes.* Somewhat hyperplastic.

MICROSCOPIC FINDINGS.—*Heart.* Negative. *Lungs.* Pulmonary abscesses. Congestion. *Spleen.* Marked congestion. No pigmented phagocytes. *Kidneys.* Congestion, otherwise negative. *Adrenals.* Excess of fat. Marked lipoidosis of fascicular and reticular zones. *Stomach.* Negative. *Intestines.* Epithelium well preserved for the greater part. No mucoid degeneration except in one portion, where the mucous glands are distended and filled with hyaline cast-like masses. Many of the glands are shallow mucous cysts. *Liver.* Cells small, simple atrophy. *Gall bladder.* Epithelium perfectly preserved. No necrosis. Papillæ less marked than normal. Submucosa edematous. *Site of injection.* Large area of necrotic muscle. Deposit of lime salts. Bacterial infection.

RABBIT 65.—Subcutaneous injection of .12 c.c. of dichlorethylsulphide. Very severe reaction. Death on the fifth day.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 23	104.3°	2750	.12 c.c. dichlorethylsulphide subcutaneously.
" 24	104.9	2580	No diarrhea.
" 25	102.0	2470	Beginning diarrhea
" 26	102.8	2410	Diarrhea.
" 27	100.8	2310	Slight diarrhea.
" 28	97.2	2200	Very severe diarrhea. Died during the night of Dec. 28 to 29.

AUTOPSY

Body cold. Marked rigor. Entire posterior portion of body is soaked with fluid feces. At the site of injection there is a small brownish area. On incising this area, the subcutaneous fascia is found to be a bright sulphur yellow in color. There is very little local edema. *Pleural cavities* and *pleuræ* are negative. The *heart* shows a slight dilatation. There is a moderate congestion of the *lungs* most marked posteriorly. The *peritoneum* is negative and there is no fluid in the abdominal cavity. The *liver* is firm, deeply fissured, and shows a marked congestion. The *gall bladder* is nearly empty, collapsed, its wall wrinkled. It contains but a few drops of a thin yellowish mucoid fluid. The *stomach* is moderately distended. The stomach mucosa appears negative. The *spleen* and *kidneys* show congestion; otherwise they are negative. *Adrenals.* Negative. The *intestines* contain only fluid fecal material. No lesions of the intestinal tract can be seen. All *splanchnic veins* show a marked congestion.

MICROSCOPIC FINDINGS.—*Heart.* Negative. Large white clot in right ventricle. *Lungs.* Intense congestion and edema. Patches of atelectasis. One of the pulmonary arteries contains a large laminated thrombus or embolus, rich in leucocytes. *Spleen.* Intense congestion. In the sinuses there are great numbers of phagocytes containing hemosiderin. *Kidneys.* Congestion, otherwise negative. *Adrenals.* In one adrenal there is an area of fibrosis. *Liver.* Intense congestion. Cloudy swelling. Cirrhosis. Coccidiosis. *Gall bladder* is completely necrotic. Necrotic diffusion zone in surrounding liver tissue. The larger bile ducts show hyaline swelling of their columnar epithelium. Excessive mucus formation. *Stomach.* Postmortem change, otherwise negative, except at the pyloric end, where there is a marked mucoid degeneration. *Intestine.* Extreme catarrh. All glands show extreme mucous degeneration. Desquamation of the epithelium. *Skin lesion.* Large area of necrosis. Hemorrhage. Edema. No reaction.

RABBIT 64.—Subcutaneous injection of .12 c.c. of dichlorethylsulphide. Severe reaction. Death on sixth day. The close parallelism between this case and the preceding is noteworthy.

DATE	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 23	103.7°	2500	.12 c.c. dichlorethylsulphide subcutaneously.
" 24	103.5	2260	No diarrhea. Some edema of abdominal wall on the right side.
" 25	103.1	2210	No diarrhea. Edema continues.
" 26	103.4	2110	" " " "
" 27	103.4	2040	Moderate diarrhea.
" 28	103.2	1920	Slight diarrhea.
" 29	97.6	1830	Marked diarrhea. Died during the night of Dec. 29 to 30.

AUTOPSY

Body cold. No rigor. Edema of abdominal wall has diminished. There is a small red-brown eschar at the site of injection. *Heart.* Moderate dilatation. Fibrin and leucocyte clot in right auricle. *Lungs* are somewhat mottled, particularly in upper lobes, probably an early lobular pneumonia. Congestion. *Peritoneum.* Moist shining. *Liver.* Congested. *Gall bladder.* Well filled. Bile, thin and greenish yellow in color. Small *intestines* and greater part of colon distended with very abundant yellowish brown fluid fecal material. Formed stools in descending colon. *Kidneys.* Moderate congestion. *Splanchnic vessels* all show marked congestion.

MICROSCOPIC FINDINGS.—*Heart.* Negative. Large white clot with very few leucocytes. *Lungs.* Purulent bronchopneumonia. Marked congestion and edema. There is a large thrombus in a pulmonary vessel, the wall of which shows necrosis. Around the vessel there is a zone of necrosis which shades off to partial necrosis, as though due to the diffusion of a necrosing substance from the vessel. There are enormous numbers of staphylococci throughout the lung. *Kidneys.* Congestion. Numerous casts in one. *Gall bladder.* Wall completely necrosed, with area of diffusion necrosis in surrounding liver tissue. *Liver.* Congestion. Cloudy swelling. Small areas of lime salt deposit in necrotic liver cells. Some of the larger bile ducts show a polynuclear infiltration around the columnar epithelium. The epithelium itself shows a slight cloudy swelling. *Adrenals.* Increased lipoid content in cortex. Congestion of medulla. *Stomach.* Negative. *Intestines.* Marked desquamative catarrh. Necrosis of upper portion of mucosa. Extreme mucoid degeneration of the glands. *Site of injection.* Enormous area of necrosis extending clear through the skin and subcutaneous tissues. Hemorrhage. Thrombosis. Areas of polynuclear infiltration. Secondary infection.

RABBIT 67.—Subcutaneous injection of .18 c.c. of dichlorethylsulphide. Very severe reaction. Severe diarrhea within 24 hours and death during the third day.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 27, 3:30 P.M.	102.2°	1660	.18 c.c. dichlorethylsulphide subcutaneously.
‘‘ 28, 11:00 A.M.	98.2	1570	Marked diarrhea. Died during the night of Dec. 28 to 29.

AUTOPSY

Body cold. Rigor mortis present. Head retracted. Fur about the anus is wet with liquid feces. The abdominal wall shows a marked edema which extends up the right flank. At the site of injection the subcutaneous tissues show but very little edema and no surface lesion is visible. Upon incising this area the fascia is found to be yellow in color. *Pleural cavities* and *pleuræ* are negative. *Heart.* Moderate dilatation. Blood coagulated. *Lungs.* Marked congestion. *Peritoneum.* Moist shining. No free fluid in peritoneal cavity. *Liver.* Congestion. *Gall bladder.* Moderately filled with thin bile. The *stomach* is partly distended. Its wall is somewhat edematous and in the mucosa several minute erosions are visible. *Spleen* and *kidneys.* Congestion. *Adrenals.* Negative. The *intestines* are distended with gas and fluid feces. Marked diarrhea. Splanchnic congestion.

MICROSCOPIC FINDINGS.—*Heart.* Negative. *Lungs.* Congestion. Some edema. Areas of atelectasis. *Spleen.* Congestion without pigmentation. *Kidneys, adrenals* and *pancreas.* Negative. *Liver.* Congestion. Slight cloudy swelling. The larger bile ducts show desquamation of the epithelium and some of them are completely necrosed. *Gall bladder.* The wall is completely necrosed and there is some necrosis from diffusion into the surrounding liver tissue. *Stomach.* Negative. *Intestines.* Catarrhal enteritis. Marked mucoid degeneration throughout.

RABBIT 66.—Subcutaneous injection of .18 c.c. of dichlorethylsulphide. Severe diarrhea. Marked fall in temperature. Death on the eleventh day.

DATE	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 27	103.7°	2550	.18 c.c. of dichlorethylsulphide subcutaneously.
‘‘ 28	102.0	2350	No diarrhea. Marked edema of abdominal wall.
‘‘ 29	101.6	2320	‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘
‘‘ 30	101.0	2260	‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘
‘‘ 31	99.6	2200	‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘
Jan. 1	99.4	2160	‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘ ‘‘
‘‘ 2	98.0	2160	No diarrhea. Edema somewhat less.
‘‘ 3	97.0	2080	Diarrhea.
‘‘ 4	97.1	1890	Marked diarrhea.
‘‘ 5	95.0	1610	Marked diarrhea. Left eye sealed with exudate. (Terminal secondary infection.)
‘‘ 6	94.0—	1540	Marked diarrhea. Both eyes sealed with mucopurulent exudate. Died during the night of Jan. 6 to 7.

AUTOPSY

Body still warm. No rigor. Both eyes sealed with exudate. When lids are separated, a large quantity of mucopurulent exudate escapes. No superficial lesion at site of injection and only a slight subcutaneous induration can be felt. There is a firm mass, about 2.5 cm. in diameter, in the abdominal wall at the site of the marked edema noted while the animal was living. On incising this mass it is found to be somewhat edematous still, and the tissues are stained a bright sulphur yellow color. *Heart.* Right-sided dilatation. *Lungs.* Pale pink in color. Slight congestion. *Liver.* Marked congestion. *Gall bladder.* Distended. Bile highly pigmented. *Stomach.* Nearly empty; its contents bile-stained and very mucoid. In the mucosa there are numerous small erosions, particularly in the fundus, along the greater curvature. These are covered with an abundant mucus and have shreds of brownish red material, probably blood clot, streaking the mucus over them. *Spleen.* Negative. *Kidneys.* Congestion and slight cloudy swelling. The *intestines* contain gas and a small quantity of fluid material. There are no formed stools. *Adrenals.* Congestion.

MICROSCOPIC FINDINGS.—*Heart.* Negative. *Lungs.* Moderate congestion. Emphysema. No edema. *Kidneys.* One kidney shows many casts in the medullary tubules. Otherwise negative. *Spleen.* Markedly congested, with a fairly large number of pigmented phagocytes. *Liver.* Congestion and cloudy swelling. *Stomach.* Extreme mucoid degeneration of the epithelium of the outer portion of the mucosa, with desquamation. Marked cloudy swelling of the parietal cells. Small postmortem erosions. *Gall bladder.* Mucosa fairly well preserved. No necrosis of wall or neighboring liver tissue. *Intestines.* Marked mucoid degeneration. Extreme catarrhal enteritis.

RABBIT 69.—Subcutaneous injection of .24 c.c. of dichlorethylsulphide. Diarrhea. Death within twelve hours.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 30, 3:45 P.M.	103.9°	1660	.24 c.c. of dichlorethylsulphide subcutaneously. No evidence of local irritation. Died during the night of Dec. 30 to 31.

AUTOPSY

Body cold. Rigor present. Soft formed stools matted in hair about anus. No superficial lesion at site of injection, only a slight subcutaneous edema. Upon incising this area there is a very strong odor of dichlorethylsulphide. *Heart.* Marked dilatation. *Lungs.* Congestion, with small hemorrhages beneath the pleura of the diaphragmatic surfaces of the lower lobes. *Liver.* Congestion. *Stomach.* Moderately distended. No lesions of mucosa visible. *Spleen, kidneys* and *adrenals.* Congestion, otherwise negative. *Intestines.* Distended with gas and fluid fecal material. No formed stools. Marked splanchnic congestion.

MICROSCOPIC FINDINGS.—*Heart.* Negative. *Lungs.* Congestion. Edema. Small capillary hemorrhages. *Adrenals.* Negative. *Spleen.* Congestion. No pigmented phagocytes. *Pancreas.* Negative. *Kidneys.* Rather marked cloudy swelling, even to simple necrosis. *Gall bladder.* Complete necrosis of wall, necrosis extending into liver tissue for some distance. Slight cloudy swelling of the liver cells. *Stomach.* Negative. *Intestines.* Congestion, otherwise negative. *Site of injection.* Large area of necrosis. Edema. No reaction.

RABBIT 70.—Subcutaneous injection of .30 c.c. of dichlorethylsulphide. Diarrhea. Death within twelve hours.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 30, 4:15 P.M.	104.0°	1810	.30 c.c. of dichlorethylsulphide subcutaneously. No evidence of local irritation. Died during the night of Dec. 30 to 31.

AUTOPSY

Body cold. Rigor present. Much soft fecal material about the anus. Strong odor of dichlorethylsulphide when area of injection is excised. *Heart.* Marked dilatation. *Lungs.* Congestion, otherwise negative. *Liver, spleen, kidneys* and *adrenals.* Congestion. *Gall bladder.* Well filled. *Intestines.* The upper portion of the small intestine is filled with yellowish fluid material. No formed stools in lower colon. Marked splanchnic congestion.

MICROSCOPIC FINDINGS.—*Heart.* Hypertrophy and dilatation. *Lungs.* Intense congestion and edema. *Spleen.* Congestion. Very few pigmented phagocytes. *Pancreas.* Negative. *Adrenals.* Congestion. *Kidneys.* Congestion and some cloudy swelling. *Liver.* Congestion and fatty degeneration. *Gall bladder.* Necrosed. Diffusion zone of necrosis in the surrounding liver tissue. *Intestines.* Epithelium well preserved. Early stage of mucous degeneration; practically every cell filled with mucus and the majority of them intact. *Site of injection.* Large eschar involving all tissues.

RABBIT 72.—Subcutaneous injection of .60 c.c. of dichlorethylsulphide. Death on the second day.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec. 31, 3:15 P.M.	102.7°	3050	.60 c.c. of dichlorethylsulphide subcutaneously. No evidence of local irritation. Animal eating in five minutes.
4:00 P.M.			Sits quietly. Respiration rate appears somewhat accelerated.
6:00 P.M.	102.5		Quiet. No diarrhea.
7:30 P.M.	102.0		Quiet. Heart regular. Respiration quickened. Seems to be about to roll over on side, but quickly recovers itself.
8:30 P.M.	101.7		No diarrhea.
9:00 P.M.	101.8		" "
9:15 P.M.			No diarrhea. Hopping about and eating.
Jan. 1, 10:00 A.M.	101.1	3010	No diarrhea.
11:00 A.M.	102.3		Soft pasty feces.
2:30 P.M.	102.5		Diarrhea.
			Died during the night of Jan. 1 to 2.

AUTOPSY

Body still somewhat warm. Perianal hair soiled. Very strong odor of dichlorethylsulphide at site of injection. *Heart.* Right-sided dilatation. *Lungs.* Congestion. *Liver, spleen, kidneys* and *adrenals.* Congestion. Otherwise negative. *Stomach.* Moderately distended. In the mucosa there are several small erosions with brownish red bases. *Intestines.* Much fluid material. No formed stools in lower colon. Diarrhea. Edema of *thoracic* and *abdominal walls.*

MICROSCOPIC FINDINGS.—*Brain.* Congestion. *Heart.* Negative. *Lungs.* Congestion without edema. *Spleen.* Intense congestion without pigmented phagocytes. *Kidneys.* Congestion. Otherwise negative. *Stomach.* Negative. Some postmortem change. *Small intestine.* Marked postmortem change, with the picture of a mucous catarrh involving the greater part of the tract. *Liver.* Cirrhosis. Coccidiosis. Large bile ducts dilated; their epithelium well preserved. The small bile ducts are unchanged. Slight fatty degeneration. *Gall bladder.* Nearly complete necrosis of wall. Narrow necrotic zone of diffusion into surrounding liver tissue.

RABBIT 74.—Subcutaneous injection of .60 c.c. of dichlorethylsulphide. .15 c.c. being injected in each of four widely separated areas on the back. Rabbit killed when dying, four hours after injection. No apparent acceleration of reaction with increased opportunity for absorption.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Jan. 1, 11:45 A.M.	103.5°	1970	.15 c.c. of dichlorethylsulphide injected in each of four areas. No evidence of local irritation.
2:15 P.M.			Lying on side. Moves legs and head readily. Heart strong and regular. The increased irritability, shown by reaction to sound and jarring of table, suggests that due to strychnine.
4:30 P.M.			Respirations few and gasping. Heart beating vigorously. Diarrhea.
4:45 P.M.			Killed by chloroform. Autopsy at once.

Autopsy

Head somewhat retracted. Perianal region covered with soft fecal material. *Heart.* Moderately dilated. *Lungs.* Negative. *Liver.* Congestion. *Gall bladder.* Nearly empty. Negative. The *stomach* is moderately distended. The mucosa of the fundus, particularly along the greater curvature, shows a large number of small, shallow erosions with dark red-brown bases. *Intestines.* Contain much fluid material. No formed stools in colon.

Microscopic Findings.—*Liver.* Marked congestion. Slight cloudy swelling. The small bile ducts are apparently normal. *Gall bladder.* Epithelium perfectly preserved. No changes observable. *Stomach.* Well preserved. Portions examined show no changes. *Intestines.* Catarrhal enteritis.

Dog 3.—White bull terrier, weight 8 kilos. Subcutaneous injection of .24 c.c. of dichlorethylsulphide. Severe diarrhea. Death in four days.

Aug. 27.—.24 c.c. of dichlorethylsulphide injected subcutaneously in back.

Aug. 28.—Appears sick. Is much less active and coat is roughened.

Aug. 29.—Appears very sick. No diarrhea.

Aug. 30.—Very severe diarrhea. Stools fluid and brownish black in color, resembling altered blood. The animal remains quiet.

Aug. 31.—12:00 noon. Lying on side. Respiration slow and shallow. Diarrhea persists.

6:00 P.M. Dog died during the afternoon. Autopsy at 7:00 P.M.

Autopsy

The body is in complete rigor. The posterior portion is soiled with fluid fecal material. At the site of injection there is an indurated lamellar area, about 10 cm. in diameter, which involves both skin and subcutaneous tissue. *Pleural cavities* and *pleuræ* negative. *Heart.* Marked right-sided dilatation, the left ventricle being in rigor. Small amount of very dark fluid blood in the chambers. *Lungs.* Free throughout. Air-containing. Middle lobe of right lung congested. No pneumonia. No free gas or fluid in *peritoneal cavity. Omentum* free. The subperitoneal vessels over the *intestines* are congested and there are a few minute subperitoneal hemorrhages. The intestines are empty and firmly contracted. The *duodenum* contains a bile-stained fluid and the mucosa is bile stained. Throughout the small intestine the mucosa shows a marked congestion and there are small hemorrhages in the summits of some of the folds. The Peyer's patches are hyperplastic. In the colon the mucosa is much congested and there are a few very minute hemorrhages. The *appendix* is negative. The *stomach* wall is contracted, the rugæ prominent. The mucosa is much congested and there are a few pinpoint hemorrhages. The *kidneys* show slight cloudy swelling. The *adrenals* are well preserved and negative. The *bladder* is contracted; its mucosa, negative.

Microscopic Findings.—The *heart* shows dilatation and its vessels are congested. *Lungs.* Marked edema. Intense congestion. Small hemorrhages. Several areas of hemorrhagic infarction, with embolic blocking of the vessels. *Spleen.* Congestion. Atrophy. *Kidneys.* Marked congestion. Slight cloudy swelling. *Pancreas.* Marked cloudy swelling. *Liver.* Cloudy swelling. Marked congestion. Marked mucoid degeneration and cloudy swelling of the epithelium of the smaller bile ducts. All of the bile ducts contain a violet-staining, hyaline substance and the epithelium is higher than normal, the cells appearing larger and swollen. The nuclei appear increased in number. The cytoplasm stains violet, but many of the cells are vacuolated. In a few of the larger bile ducts there are small areas of necrosis. The *stomach* mucosa is intact. There is marked congestion and some increase in mucus in the upper portion of the mucosa. The mucosa of the small *intestine* is congested, edematous, and infiltrated with leucocytes. The epithelium of the glands shows syncytial formations of regenerating epithelium. The columnar form of the cells is lost and there is no mucus formation except in the lower small intestine, where there are many mucous cysts, especially in the deeper portions of the mucosa. The fundi of the glands of Lieberkühn are dilated, filled with stringy mucin or a colloid material. The epithelium is cuboidal, or flattened, or syncytial, and stains a deep violet with hematoxylin and eosin. In some of the dilated glands of Lieberkühn the epithelium is entirely gone and the lumen is filled with a hyaline cast. The epithelium of the upper part of the glands and of the surface is entirely gone. The picture is that of a severe degenerative and desquamative catarrhal enteritis with beginning regeneration. The lymph follicles are hyperplastic and the germ centers show lymphoid exhaustion. *Mesenteric nodes.* Marked congestion. Great numbers of hemophages filled with blood cells. *Adrenals.* Marked congestion of medulla. *Site of injection.* A large eschar with marked edema. In the vessels there are large thrombi. The borders of the lesion show an abundant polynuclear infiltration and large areas of hemorrhagic extravasation.

(b) Subcutaneous Injection of Hydrochloric Acid

Since it has been assumed by some that the local and general effects of dichlorethylsulphide are due to the action of the hydrochloric acid produced by its hydrolytic cleavage, a series of animals was given varying amounts of hydrochloric acid by subcutaneous injection. The following protocol is selected as illustrative of this group.

Rabbit 76.—Subcutaneous injection of .60 c.c. of hydrochloric acid. Both local and general reactions entirely unlike those produced by dichlorethylsulphide.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Jan. 3, 9:45 A.M.	103.2°	1600	.60 c.c. of hydrochloric acid subcutaneously. Very marked evidence of local irritation. Marked contraction of superficial and deep muscles. The skin "knots up." In about five minutes, evidences of severe pain cease and the animal is eating.
4	103.6	1710	No diarrhea. Very extensive lesion at site of injection. There has been complete destruction of the skin and subcutaneous fascia over an area 4 by 5 cm., so that the muscles of the back are fully exposed.
5	103.4	1600	No diarrhea. The muscle is now exposed over an area 5 by 7 cm. There is a constant oozing of blood from the borders of the deeply excavated lesion.
6	103.8	1490	No diarrhea. Still some bleeding from wound.
6, 8:30 P.M.			Killed by chloroform. Autopsy at once.

AUTOPSY

Large excavated lesion, measuring 5 by 7 cm., at the site of injection. The borders are smooth. The base consists of charred, dry, fragmented muscle in coarse bundles and masses. There is no purulent exudate. The whole lesion is nearly black in color, as though charred, and is very foul smelling, with the odor of dry gangrene. *Heart.* Still beating. Negative. *Lungs.* Bright pink in color. Moderate congestion. *Liver.* Congested. Extensive coccidiosis. *Spleen.* Negative. *Stomach.* Contains a small amount of food and water, and much swallowed mucus. There are no visible lesions of the mucosa. The *intestines* are nearly empty except the cecum which is moderately filled. The scant amount of fecal matter in the small intestine is very thin, mucoid, and bile stained. In the lower colon the fecal material is soft and but slightly formed. There is, however, no evidence of diarrhea about the anus.

MICROSCOPIC FINDINGS.—*Heart.* Negative. *Lungs.* Congestion. No edema and no hemorrhages. *Liver.* Coccidiosis. No diffusion necrosis into liver tissue around the gall bladder. *Gall bladder.* Epithelium well preserved. No necrosis. No desquamation. Many mucin threads in lumen. *Stomach, intestines, kidneys* and *adrenals.* All negative. *Tissue from site of injection.* Very extensive eschar formation.

(c) SUBCUTANEOUS INJECTION OF DIHYDROXYETHYLSULPHIDE

A series of animals was given varying doses of dihydroxyethylsulphide (hydrolyzed mustard gas) by subcutaneous injection, in order to ascertain whether the severe general effects could be due to the absorption of this substance from the site of injection. The following condensed protocols are selected from this series.

RABBIT 80.—Subcutaneous injection of .30 c.c. of dihydroxyethylsulphide. No local lesion, no diarrhea and no loss of weight.

DATE	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Jan. 8	104.6°	2250	.30 c.c. of dihydroxyethylsulphide subcutaneously. No evidence of local irritation, and animal eats at once when released.
" 9	102.8	2210	No diarrhea. No local lesion.
" 10	102.6	2270	" " " " "
" 11	102.8	2240	" " " " "
" 12	101.9	2250	" " " " "
" 13	102.6	2300	" " " " "
" 14	102.0	2300	" " " " "
" 15	101.6	2280	" " " " "
" 17	104.0	2170	" " " " "
" 18	103.6	2180	" " " " "

RABBIT 81.—Subcutaneous injection of .60 c.c. of dihydroxyethylsulphide. No local lesion. No diarrhea.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Jan. 8, 9:25 P.M.	104.6°	2110	.60 c.c. of dichlorethylsulphide subcutaneously. No evidence of local irritation, and animal eats at once when released.
" 9, 8:30 A.M.	103.2	2100	No diarrhea. Very slight edema at site of injection.
2:30 P.M.			No diarrhea.
2:45 P.M.			Killed with chloroform. Autopsy at once.

AUTOPSY

There is a slight congestion of all organs. *Stomach* is well filled, its mucosa grossly negative. *Intestines.* Apparently negative. Formed feces in lower colon. No evidence of diarrhea. The *bladder* contains a very turbid yellowish white urine. No other changes.

MICROSCOPIC FINDINGS.—*Lung.* Slight congestion. No edema. *Kidneys.* Negative. Slight congestion. *Adrenals.* Negative. *Spleen.* Negative. *Liver.* Marked fatty change. *Gall bladder.* Epithelium perfectly preserved. No changes. *Small intestine.* Slight, but well defined catarrh. Congestion of mucosa. Excessive mucus formation. *Stomach.* Negative.

(D) INTRAVENOUS INJECTION OF DICHLORETHYLSULPHIDE

The following condensed protocols are selected from the various series of intravenous injections. In every case in which dichlorethylsulphide was given, it was injected without dilution. Although bland oils will serve as suitable diluents so far as mutual solubility is concerned, the certainty of producing some degree of fatty embolism, with resulting confusion in the pathologic picture, renders this method inadvisable. In addition, the much greater solubility of dichlorethylsulphide in the oil than in the body fluids may be expected to retard its action and delay the production of its characteristic symptomatology.

RABBIT 53.—Intravenous injection of .06 c.c. of dichlorethylsulphide. General convulsions. Marked reduction of temperature. Prostration. Death in less than three hours.

TIME	TEMPERATURE DEGREES	WEIGHT IN GM.	NOTES
Dec 9, 2:50 P.M.	101.5°	1570	.06 c.c. of dihydroxyethylsulphide given intravenously in superficial femoral vein. Light chloroform anesthesia. Animal made quick recovery from anesthesia, soon moving about.
3:50 P.M.	94.0		Animal very much weaker. Respiration very rapid. Easily startled by sudden movements or unexpected noises. Slight convulsive movements. No general convulsion.
3:54 P.M.			First general convulsion, consisting of irregular rapid movements. There is some opisthotonos but the head is drawn chiefly to one side.
4:15 P.M.			Lies on side. Occasional convulsions.
4:45 P.M.			Continues to lie on side. Can not turn over. Jerking movements of forepaws, head and neck. Salivation and lacrimation. Pupils dilated. Respiration slow and irregular.
5:30 P.M.			Death. Much stringy saliva during last fifteen minutes.
8:00 P.M.			Autopsy.

AUTOPSY

Body nearly cold. Rigor mortis marked. Abdomen moderately distended. No diarrhea. *Pleural cavities* and *pleuræ* negative. *Heart.* Moderately dilated, particularly on the right side. Dark fluid blood, clotting tardily. *Lungs.* Air-containing throughout. Congestion moderate, except posteriorly. *Spleen.* Negative. *Kidneys.* Slight congestion. *Adrenals.* Negative. *Liver.* Marked congestion. Lobules large. Central zones dark red, outer two-thirds of lobule, grayish red. *Gall bladder.* Well filled with a pale mucoid bile. *Stomach.* Distended with food. Mucosa shows scattered areas of postmortem change along greater curvature. Upper small *intestines* contain a thin yellowish mucoid fluid. Lower small intestine is well filled and there are formed stools in the lower colon.

MICROSCOPIC FINDINGS.—*Central nervous system.* Congestion. *Heart.* Negative. *Lungs.* Congestion. Atelectasis. No edema. No hemorrhage. *Spleen.* Marked congestion but no pigment. *Adrenals* and *pancreas.* Acute congestion. *Stomach.* Slight cloudy swelling of parietal cells. Congestion. *Intestines.* In portion examined the mucosa is well preserved. Congestion of villi. No necrosis. *Liver.* Moderate congestion Slight fatty degeneration.

Rabbit 51.—Accidental intravenous injection of dichlorethylsulphide in the course of a deep subcutaneous injection. Total injection .12 c.c., of which probably less than .06 c.c. entered a small subcutaneous vein. Convulsions. Diarrhea. Death in four hours.

Autopsy

Body still warm but rigor mortis is present. Soft fecal material from anus. Posterior portion of body is much soiled with feces. *Pleural cavities* and *pleuræ.* Negative. *Heart.* Right-sided dilatation. Blood, fluid, clotting slowly. *Lungs.* Free. Slight congestion. Air-containing throughout. *Spleen.* Negative. *Kidneys.* Moderate congestion. *Adrenals.* Negative. *Liver.* Moderate congestion. *Stomach.* Distended with food. The first portion of the small *intestine* contains a very abundant slightly yellow fluid, which is somewhat mucoid. In the descending colon and rectum there are no formed stools.

Microscopic Findings.—*Heart.* Negative. *Lungs.* Moderate congestion. No edema. Small patches of atelectasis. Bronchioles dilated. No hemorrhages. *Spleen.* Moderate congestion with few pigmented cells. *Kidneys.* Congestion. *Intestine.* Mucosa well preserved. *Stomach.* Negative. *Liver.* Congestion. Slight cloudy swelling.

(e) Intravenous Injection of Hydrochloric Acid

Rabbit 89.—Intravenous injection of .06 c.c. of hydrochloric acid. Animal living on fourth day. No diarrhea. No evidence of general reaction.

Time	Temperature Degrees	Weight in gm.	Notes
Jan. 16, 11:45 A.M.	103.0°	1520	.06 c.c. of strong hydrochloric acid (diluted to 1.20 c.c. with distilled water) in jugular vein.
1:00 P.M.			Apparently well.
Jan. 17	102.4	1710	No diarrhea.
" 18	103.4	1680	" "
" 20	104.6	1600	No diarrhea. Perfectly well.
" 20			Killed. Autopsy at once.

Autopsy

Gross findings all negative, except thrombosis of jugular at site of injection.

Microscopic Findings.—All negative, except for thrombophlebitis at site of injection.

(f) Intravenous Injection of Dihydroxyethylsulphide

Rabbit 87.—Intravenous injection of .30 c.c. of dihydroxyethylsulphide. Animal living on the fifth day. No diarrhea. No marked loss of weight.

Time	Temperature Degrees	Weight in gm.	Notes
Jan. 15, 4:00 P.M.	101.6°	2410	.30 c.c. of dihydroxyethylsulphide into jugular vein. Light chloroform anesthesia.
7:00 P.M.			Animal eating. Apparently well.
Jan. 16	103.9	2350	No diarrhea.
" 17	102.6	2320	" "
" 18	102.4	2320	" "
" 20	102.3	2350	No diarrhea. Perfectly well.
" 20			Killed. Autopsy at once.

Autopsy.—All gross findings negative.

Microscopic Findings.—Negative, except for marked fatty liver.

SUMMARY OF EXPERIMENTAL WORK

Subcutaneous Injections.—When pure dichlorethylsulphide is injected subcutaneously in doses of from .015 up to .60 c.c., the injections are apparently painless and the animals exhibit no signs of discomfort. Even with the largest doses the animals resume feeding as soon as released and give no evidence of local irritation. At varying periods of time, from one hour to several days, depending in part upon the size of the dose, and in part upon the rate of absorption, toxic symptoms appear, usually in the form of salivation, diarrhea and marked depression of temperature. At first the respirations are quickened; later they become slow. From the largest doses the animal may die within two hours, without diarrhea, but with a short period of nervous excitement followed by coma and gradual failure of respiration. Doses of from .015 to .06 c.c. are not necessarily fatal to rabbits, although a certain proportion of the animals receiving such doses do die. Death from these doses usually takes place from the fourth to the tenth day. Diarrheal symptoms may appear as early as the second day, but in the great majority of cases diarrhea does not appear until the fourth to seventh day. Coincident with the diarrhea there is a marked fall of temperature, which may be as much as seven to eight degrees below normal. If the animal survives the diarrheal period, the temperature may come back nearly to, or quite to, normal, to fall again just before death, if the animal dies. During the diarrheal stage the animal rapidly loses weight and this loss of weight continues after the cessation of diarrhea, so that when the animal dies, it may have lost as much as one-third of its body weight. The diarrheal stools are

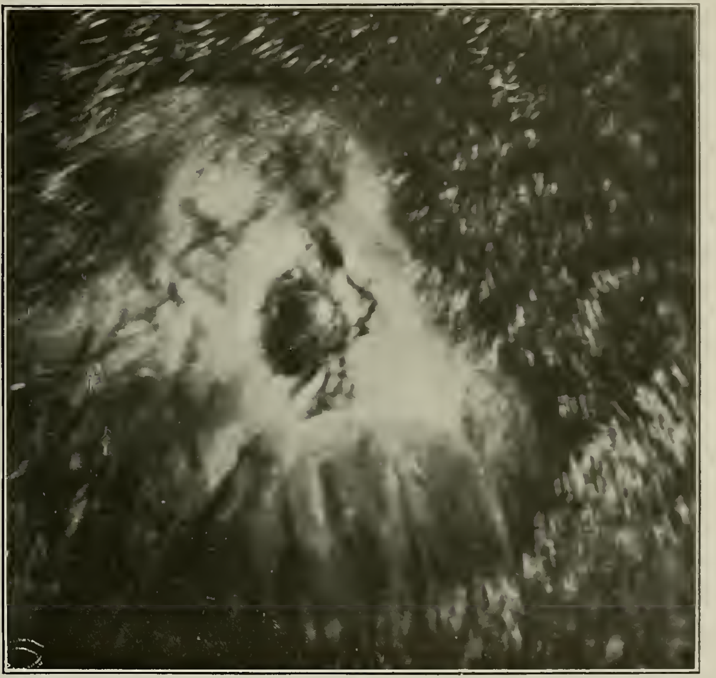

Fig. 131.—Rabbit 58. Eschar resulting from subcutaneous injection of .03 c.c. of dichlorethylsulphide, eighteen days after injection.

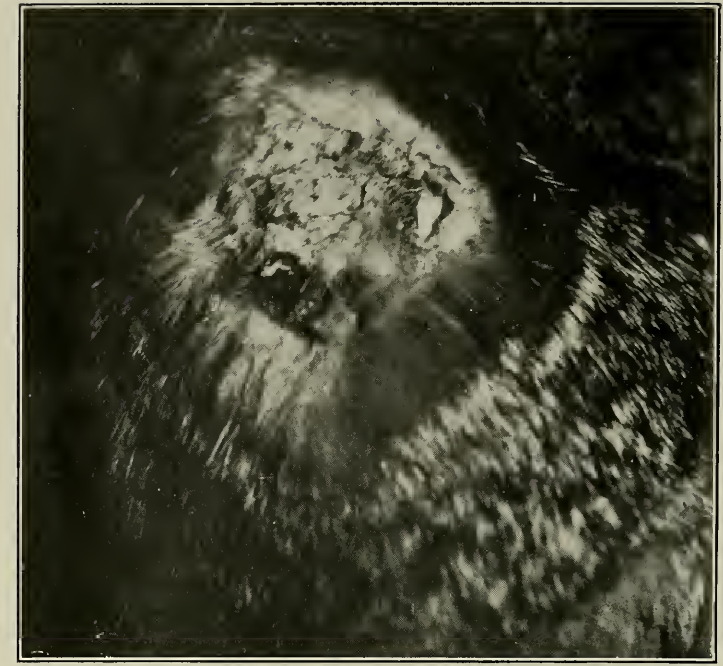

Fig. 132.—Rabbit 62. Eschar resulting from subcutaneous injection of .06 c.c. of dichlorethylsulphide, eleven days after injection.

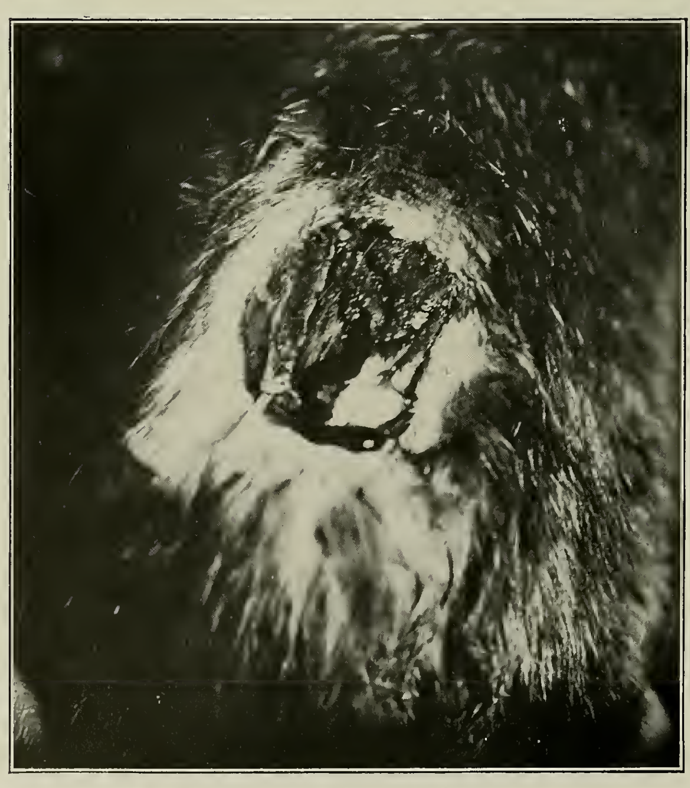

Fig. 133.—Rabbit 76. Sloughing lesion produced by subcutaneous injection of .60 c.c. of hydrochloric acid, twenty-four hours after injection.

fluid, mucoid, brown to black, sometimes tarry, and very foul smelling. Accompanying the diarrhea, there is a marked anorexia and great thirst; the animal is quiet, depressed; and both circulation and respiration are slowed. In the animals that recover, the diarrhea may last for several days, accompanied by a marked lowering of temperature and a general depression. As the stools become normal the temperature rises and the general condition improves until the animal is again apparently perfectly normal.

At the site of the subcutaneous injection there develops a local edema which is usually much less than the edema produced by cutaneous applications. In a certain number of cases, there is a marked edema of the belly wall, although the injections were routinely made on the back of the animal, apparently due to the hypostasis of body fluid containing mustard gas, from the seat of the injection. The edematous area at the seat of injection gradually changes into an indurated eschar (see Figs. 131 and 132) which undergoes a slow demarcation from the neighboring living tissue. In some animals injected subcutaneously with the dichlorethylsulphide furnished by the Chemical Warfare Service and living two days or longer, a sulphur-yellow coloration of the tissue at site of injection was noted. Such a coloration was not noticed in any animal injected with the Gomberg preparation.

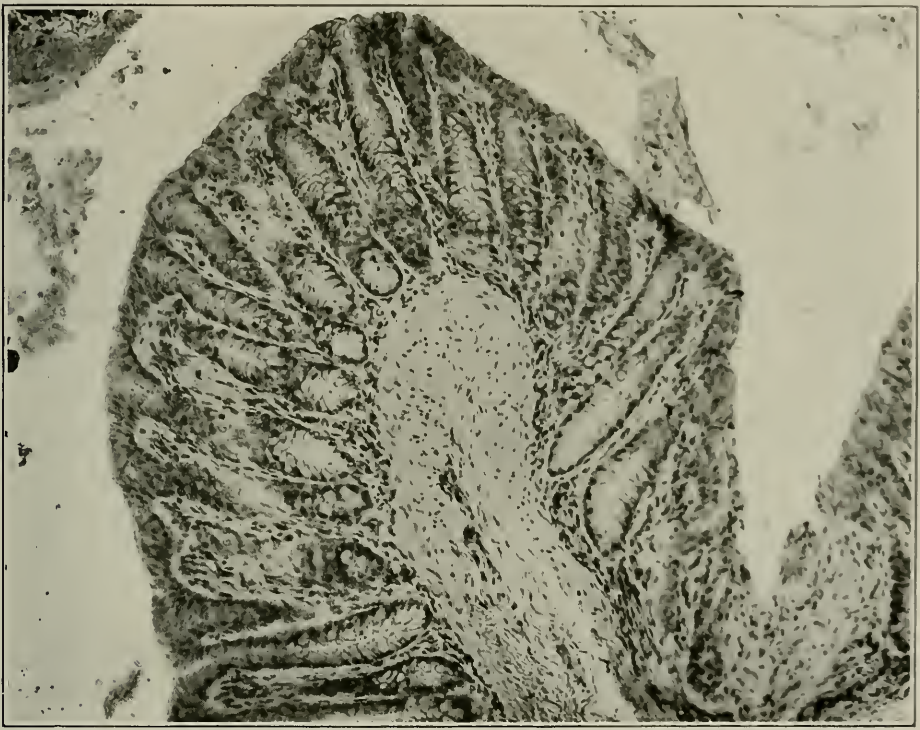

Fig. 134.—Rabbit 59. Received subcutaneous injection of .045 c.c. of dichlorethylsulphide. Died on third day during mild diarrhea. General mucoid degeneration.

The gross pathology shown by animals killed or dying at varying periods after subcutaneous injections consists of a general passive congestion of all organs with occasional minute hemorrhages, emboli, and infarctions. The most

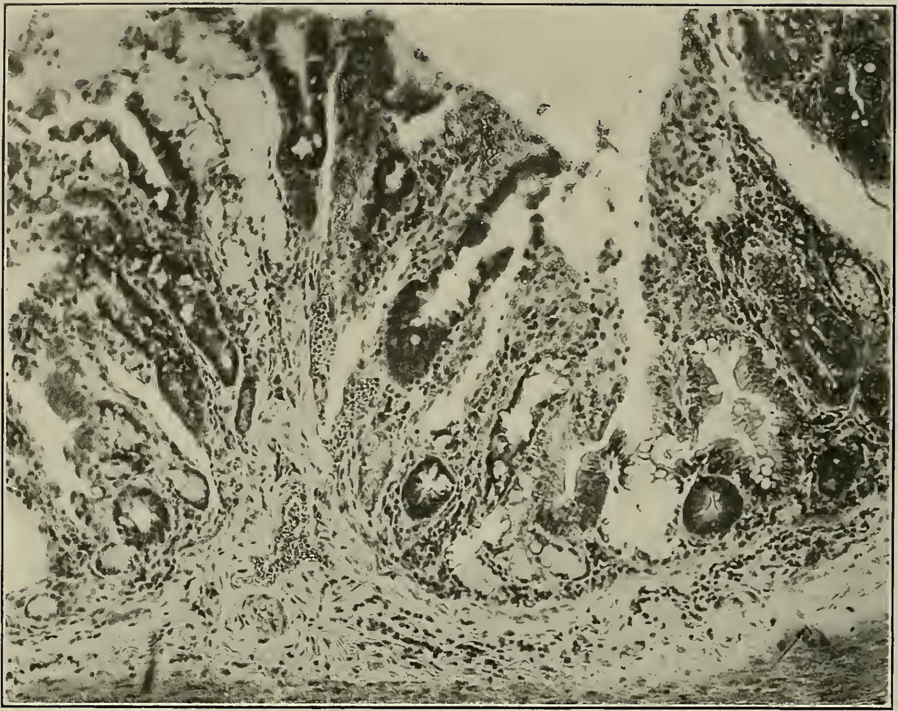

Fig. 135.—Rabbit 66. Received subcutaneous injection of .18 c.c. of dichlorethylsulphide. Began to have diarrhea seven days after injection and died four days later. Section of upper portion of small intestine showing acute catarrhal enteritis.

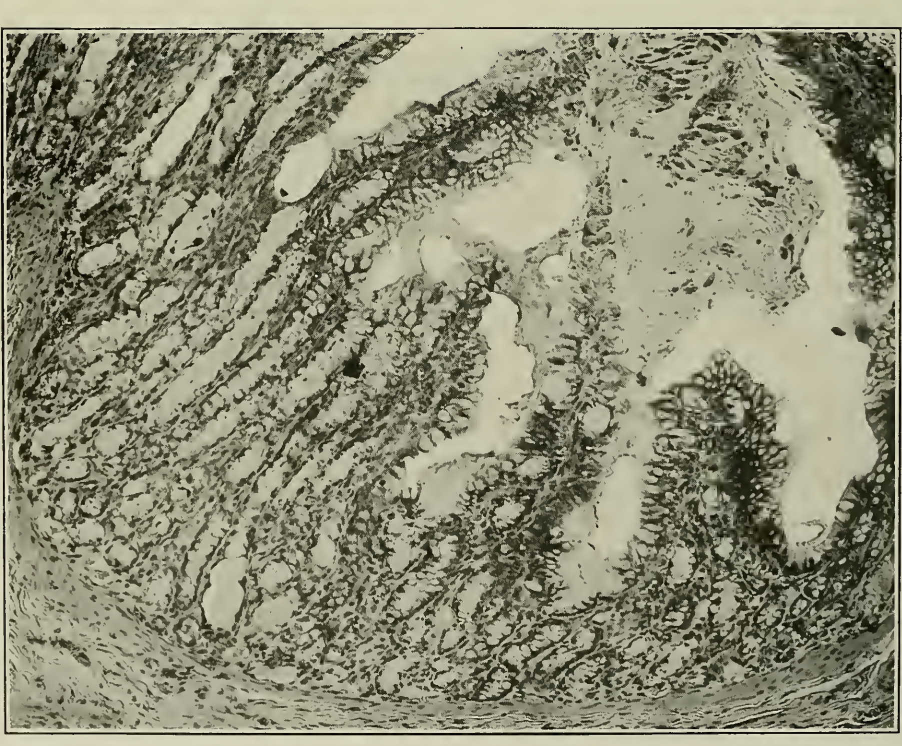

Fig. 136.—Same rabbit as preceding. Extreme mucoid degeneration. Catarrhal enteritis. Mucous diarrhea.

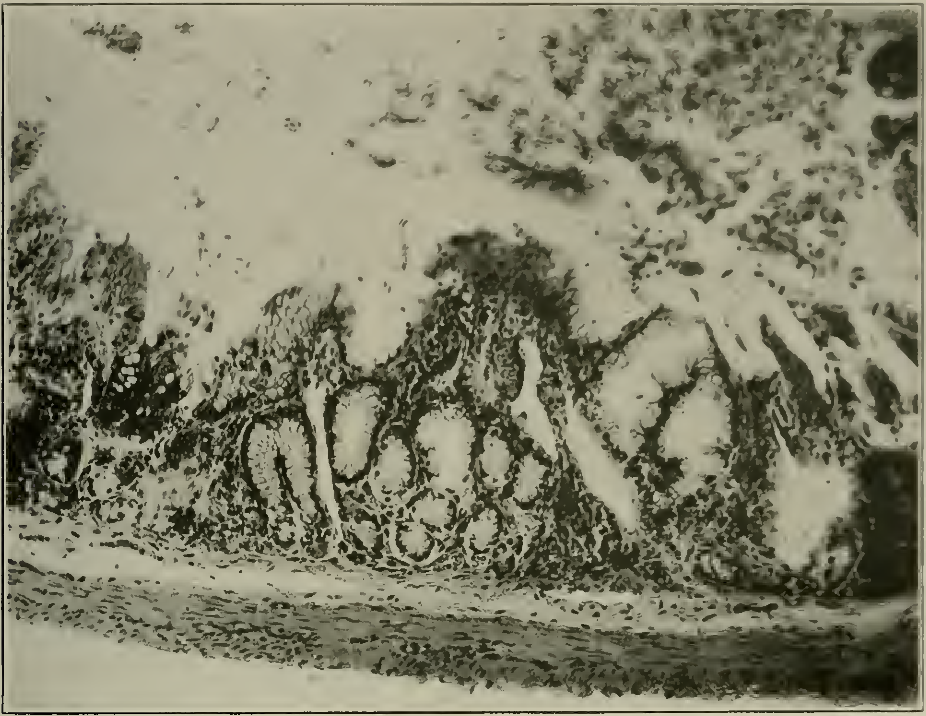

Fig. 137.—Section of cecal wall from same rabbit as preceding. Marked catarrhal inflammation. Mucous diarrhea.

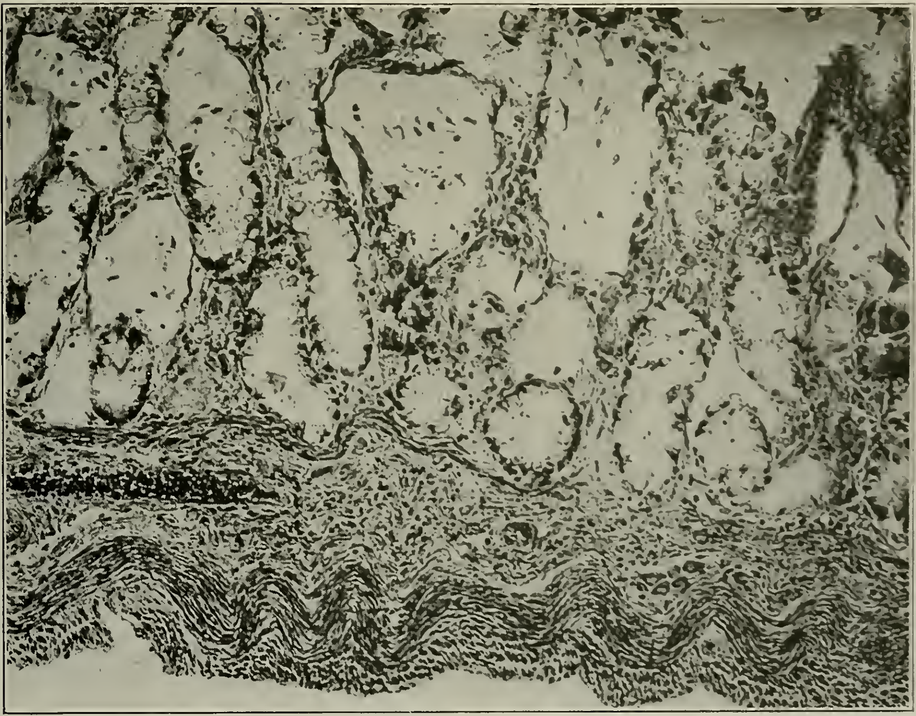

Fig. 138.—Rabbit 65. Received subcutaneous injection of .12 c.c. of dichlorethylsulphide. Diarrhea began on the second day, the animal dying three days later. Extreme mucoid degeneration of the entire intestinal epithelium. Mucous diarrhea.

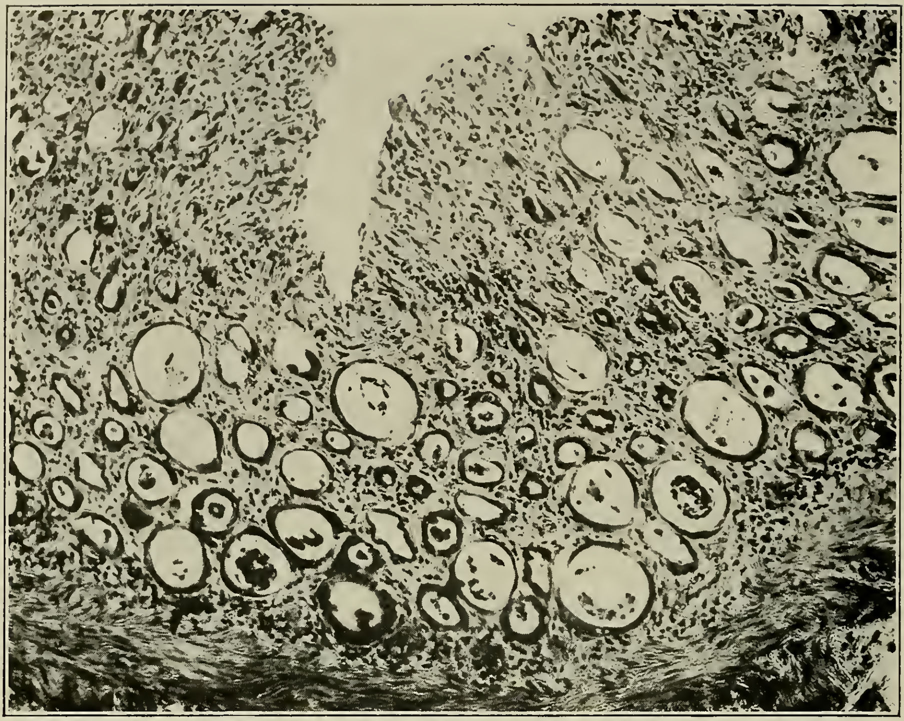

Fig. 139.—Dog 3. Received subcutaneous injection of .24 c.c. of dichlorethylsulphide. Died in four days with a very severe diarrhea. Extreme catarrhal desquamative enteritis. Mucoid degeneration and necrosis of the glandular epithelium.

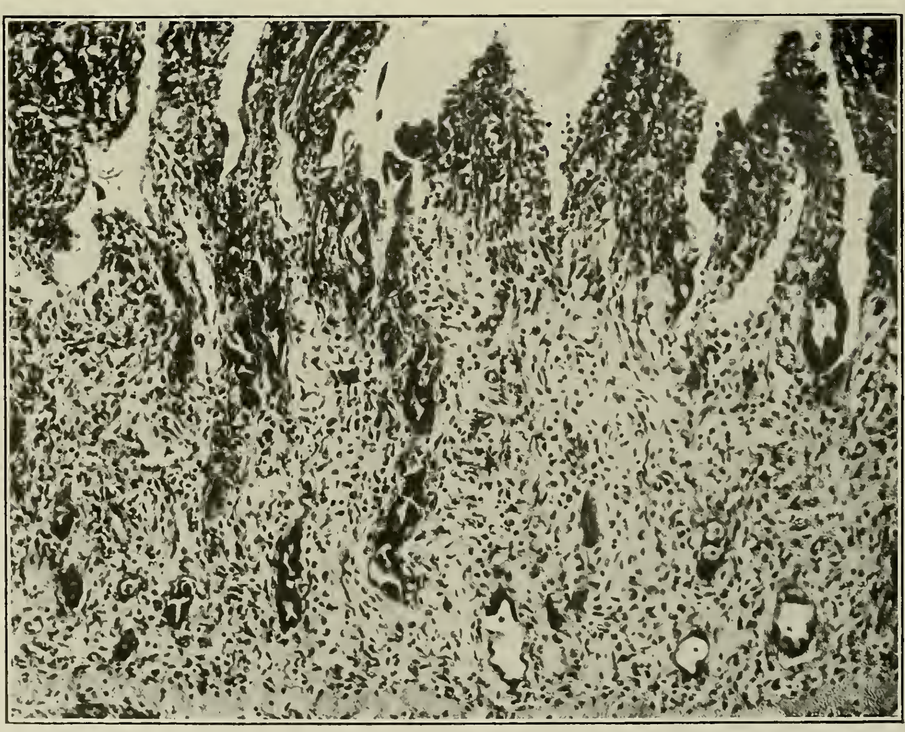

Fig. 140.—Same dog as preceding. Middle portion of small intestine showing desquamation of the superficial epithelium and necrosis of the epithelium of the glands of Lieberkühn. Severe enteritis.

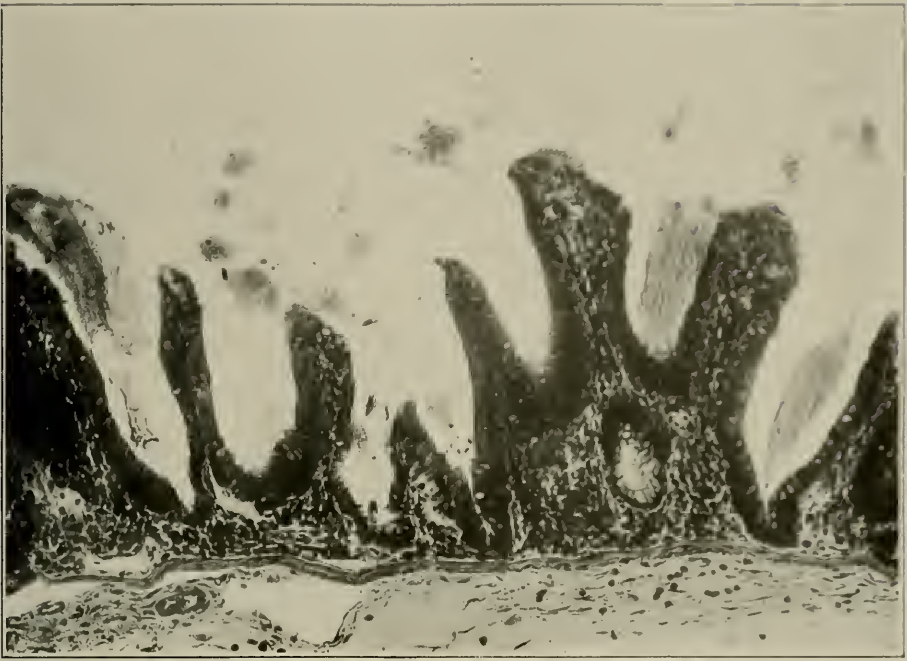

Fig. 141.—Rabbit 63. Received subcutaneous injection of .06 c.c. of dichlorethylsulphide. Severe diarrhea from fourth to ninth day. Killed fifteen days after injection. Mucosa of intestine intensely congested and edematous. Marked mucoid degeneration with cystic glands. Regeneration of superficial epithelium.

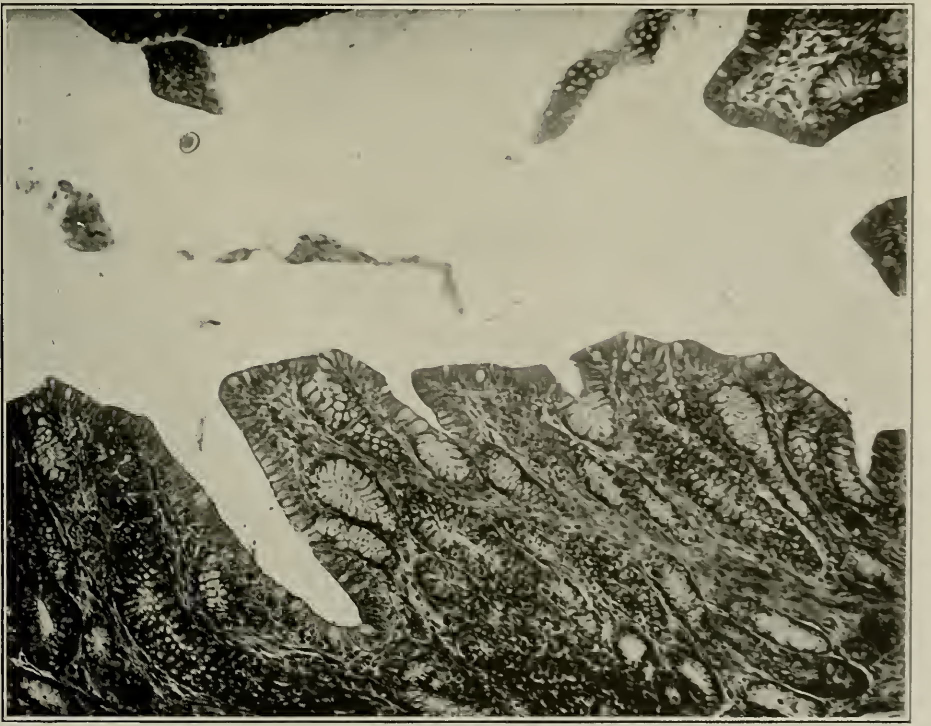

Fig. 142.—Rabbit 50. Received subcutaneous injection of .06 c.c. of dichlorethylsulphide. Very severe diarrhea on fifth to seventh day afterwards. Apparent recovery. Killed on the thirty-second day after injection. Mucosa shows excessive mucus formation.

specific changes are those found in the gastrointestinal tract in the form of an intense splanchnic congestion and a more or less severe catarrhal enteritis. In practically every instance it was noted that the contents of the gall bladder consisted of a thin, pale, yellowish, mucoid bile.

The microscopic findings confirm the gross appearances. No specific changes are found in any organs except the intestines, spleen, and possibly the bile ducts. These specific changes consist in a mucoid degeneration, necrosis, and desquamation of the epithelium of the intestinal mucosa, marked congestion of the whole splanchnic area, with edema, and occasional petechial hemorrhages and minute erosions of the mucosa. Degenerative changes have also been noted in the epithelium of the bile ducts, and the postmortem changes in the mucosa of the gall bladder and larger bile ducts appear to be greatly hastened, and more severe than normal, as though from the presence of some necrosing substance in the bile. (See Figs. 134 to 143.) A very striking feature of the pathology of many cases of subcutaneous injections of dichlorethylsulphide is the presence in the blood spaces and sinusoids of the spleen of great numbers of large pigmented phagocytes and hemophages containing altered red blood cells, indicating a greatly increased hemolysis. (See Fig. 143.)

The microscopic appearances of the tissues at the site of injection are those of an extensive eschar extending entirely through the skin and fascia, and deep into the muscles with extensive extravasations and infiltrations of leucocytes. The appearances of secondary infection are frequently added to those of the primary lesion. In several instances deposits of lime salts were noted in the necrotic area.

Intravenous Injections.—When dichlorethylsulphide is injected directly into the external jugular or superficial femoral veins in doses varying from .0075 to .18 c.c., the animal shows no signs of pain and returns to eating, but within a short time begins to show symptoms of hyperexcitability in the form of very rapid respiration and slight convulsive movements. Within an hour there may be general convulsions and opisthotonos with head turned to one side. The animal quickly becomes very weak, tends to lie upon its side with rapid jerking movements of the legs, as though running. The animal can not turn over. Soft feces are frequently involuntarily discharged. The animal acts as though nauseated and there are slight salivation and lacrimation. The pupils are dilated. The temperature rapidly falls six to eight degrees before death. The convulsions cease, the pupils contract, salivation increases, the animal passes into coma, and there is a gradual failure of circulation and respiration, although the respiration ceases some time before the heart stops beating. Death usually takes place in one to four hours, depending upon the size of the dose. Following the intravenous injection of larger doses, the first convulsive movements may appear in ten minutes and be followed rapidly by wild clonic convulsions, very much resembling those of rabies.

The gross pathologic changes following intravenous injections of dichlorethylsulphide are dilatation of the heart, particularly on the right side, and marked congestion of the lungs with numerous petechial hemorrhages. All other organs show congestion with numerous minute hemorrhages. Mucosa of gastrointestinal tract is covered with thick mucus, is congested, and may show minute hemorrhages. The contents of the gall bladder may be a thin and pale bile. No specific changes were found in the brain and cord and no thrombus in the vein at the site of injection.

Microscopic examination confirms the gross appearances, in that it shows extreme congestion, stasis and hemorrhages in the lungs; congestion of the gastrointestinal tract, with an increased formation of mucus scattered irregularly throughout, not comparable, however, to the changes found in animals injected subcutaneously; and marked general congestion.

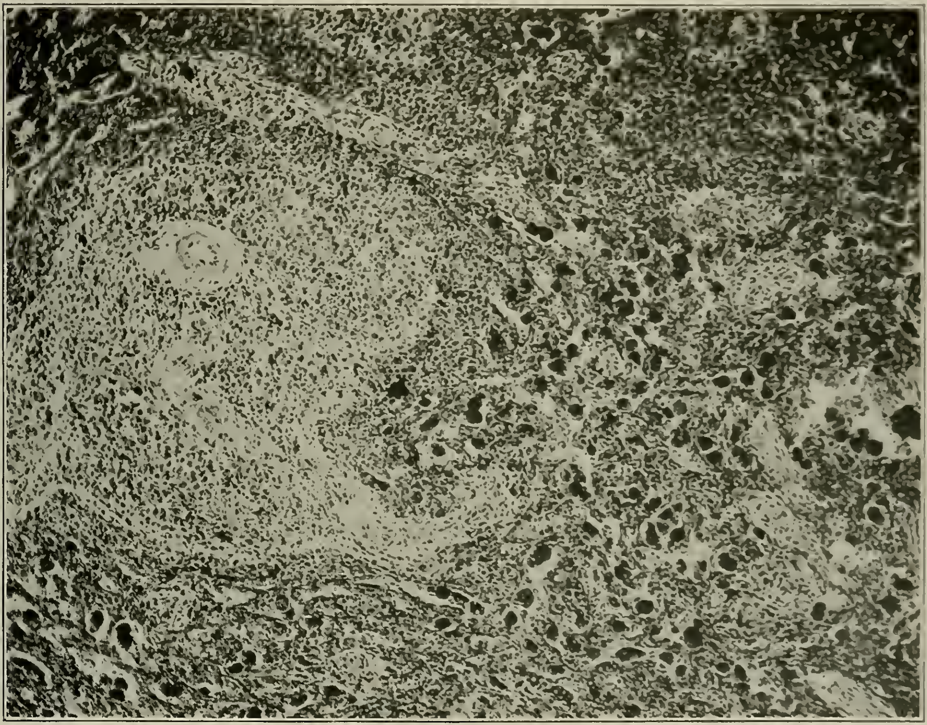

Fig. 143.—Rabbit 47. Received subcutaneous injection of .03 c.c. of dichlorethylsulphide. Very severe diarrhea on fourth to eighth day. Died on twelfth day after injection. Intestines showed severe catarrhal enteritis. Section of spleen showing the great number of pigmented phagocytes in the blood sinuses.

EPICRISIS

The introduction of dichlorethylsulphide into the blood stream causes death within a few hours with characteristic symptoms. When injected subcutaneously, with resulting slower absorption into the circulation, death occurs later, from twelve hours to several days, likewise with a characteristic symptomatology. The symptoms may be classed roughly as (1) nervous and (2) intestinal. In the case of large doses, with death occurring within an hour, the nervous symptoms alone may be exhibited, while in the animals living for some time the nervous symptoms are slight and those of the intestinal group predominate. In the correlation of the pathologic findings with the symptomatology, no change has been found in the central nervous system offering an adequate explanation for a death dependent entirely upon a lesion of the central nervous system. In the delayed cases (subcutaneous) the intestinal tract offers a pathologic picture commensurate with the symptoms. In addition to the specific pathology just mentioned, incidental pathologic findings in the form of thrombi, emboli, embolic infarctions and hemorrhages may at times be interpreted as explaining some of the observed clinical phenomena.

Of all the pathologic lesions produced by mustard gas, apparently the most specific and most interesting are the intestinal changes following intravenous and subcutaneous injections. The intense catarrhal enteritis observed after such injections suggests the excretion of dichlorethylsulphide or some product of its decomposition through the intestinal mucosa. No changes have ever been observed in the kidneys, indicating the excretion of any toxic product through the renal epithelium. In the case of the liver there have been observed, at times, degenerative changes in the biliary epithelium, suggesting the presence of some injurious substance in the bile. Further, the probability of this hypothesis seems the greater in view of certain changes, found in a certain proportion of cases, in the gall bladder, in the form of an apparently earlier postmortem necrosis of the gall bladder wall, and a diffusion of the bile into the neighboring liver tissue. It has been a notable observation that, in many cases, when autopsy was performed immediately upon death of the animal, such early postmortem change was found in the gall bladder; while in animals that had not received dichlorethylsulphide injections, such an immediate postmortem change was not observed.

A large number of experiments were made in the effort to demonstrate the presence of mustard gas or its products in the intestinal wall and contents, and in the liver and bile. In the tissues at the site of the injection, the odor of mustard gas will persist for several days and cutaneous applications of the ether extract of these tissues will produce a well-marked mustard burn, even when the ether extract is much diluted. Further, in one case in which death occurred within one hour after jugular injection, with numerous small embolic hemorrhages in the lungs, the odor of mustard gas was clearly evident on section of the lung, and an ether extract of the lung gave a slight positive test. With this single exception we have been unable to obtain any odor of mustard gas or any positive skin reaction from extracts of any organ. Ether and aqueous extracts of the liver and bile, the intestinal tract and its contents, the blood, heart and lungs, and of the urine, even when concentrated, have yielded no odor of mustard gas and have given no positive skin test

It has been generally assumed that the injurious action of mustard gas follows its hydrolysis in the living cells and tissues. The products resulting from the hydrolysis of dichlorethylsulphide are hydrochloric acid and dihydroxyethylsulphide.

From Major Moses Gomberg of the Chemistry Department of the University of Michigan a quantity of pure dihydroxyethylsulphide was obtained. Varying series of experiments made with this substance showed it to be apparently inert, both as applied locally, by ingestion, and by subcutaneous and intravenous injections, in quantities up to many times the lethal doses for dichlorethylsulphide. No diarrhea, no fall in temperature, and no other symptoms were produced, and no pathologic lesions were found in such animals with the exception of marked fatty changes in the liver cells.

A similar set of experiments with hydrochloric acid injections was also carried out. The subcutaneous injection of hydrochloric acid, even in a dose of .12 c.c. produces intense local irritation and pain, in striking contrast to the anesthetic action of dichlorethylsulphide. The course of the local lesion is entirely unlike that produced by mustard gas. The liquefaction of the eschar is very rapid and there quickly results a deep excavated lesion, the bottom and sides of which appear charred. (See Fig. 133.) No diarrhea is produced; the temperature remains normal or rises; no systemic symptoms are produced, and the animal will recover unless secondary infection sets in.

The intravenous injection of .06 c.c. of hydrochloric acid (diluted to prevent local injury during injection) produces no symptoms comparable to those resulting from the intravenous injection of dichlorethylsulphide.

The manner of causation of the intestinal lesions remains the special problem of the pathology of dichlorethylsulphide poisoning. Neither hydrochloric acid nor dihydroxyethylsulphide, when introduced into the circulation, will cause similar changes. Therefore these lesions can not be the result of the action of hydrochloric acid produced at the site of the lesion and circulating in the blood. The next most plausible explanation of the cause of the intestinal lesions is that mustard gas itself or some other unknown decomposition product circulates in the blood and is excreted through the mucosa of the intestine, or possibly, also, through the bile.

It has been stated that the most delicate chemical test for mustard gas is a color reaction with a solution of platinic chloride and sodium iodide. The liquid to be tested is applied to absorbent paper moistened with this solution. In the presence of dichlorethylsulphide the pink color is changed to a faint purple, which becomes blue or deep blue, depending upon the concentration of the mustard gas solution. When this test was applied to ether and aqueous extracts of the liver, bile and intestine from animals injected subcutaneously and intravenously with dichlorethylsulphide, we obtained a definite blue color more marked in the case of the aqueous extracts. This reaction we at first believed to be a positive test for mustard gas in these extracts. Continuing our control experiments, we found that the dihydroxyethylsulphide gives the same reaction with the platinic chloride-sodium iodide as dichlorethylsulphide. The test is, therefore, not a specific one for pure dichlorethylsulphide. We then took the aqueous extracts of liver, bile, intestine and urine, which might be expected to have the dihydroxyethylsulphide in them, if it were present at all, since it is soluble in water, and heated them with concentrated hydrochloric acid with the expectation of reconverting the hydrolyzed product into mustard gas. The products thus obtained, however, gave no odor of mustard gas, and their ether extracts neither gave a skin reaction nor a positive color test. On the other hand, these aqueous extracts of body fluids and organs did give bluish green color tests with the test solution that might be interpreted as faint positive reactions for mustard gas. Unfortunately, however, the aqueous extracts of these same organs and fluids from animals untreated with mustard gas produce an identical color reaction. We have, therefore, been unable to demonstrate the presence of mustard gas or its hydrolyzed products in the liver, bile, intestines, feces, blood or urine.

CONCLUSIONS

1. Dichlorethylsulphide when injected internally in doses of approximately .06 c.c. per kilo for the rabbit, and .03 c.c. per kilo for the dog, causes a fatal intoxication, characterized, when death occurs quickly, by symptoms referable to the central nervous system; but when death takes place more slowly, by intense diarrhea, anorexia and reduction of temperature.

2. The only specific pathology of such fatal poisonings is a marked degeneration of the epithelium of the gastrointestinal tract in the form of a severe catarrhal enteritis, and the occasional occurrence of similar changes in the epithelium of the bile ducts and gall bladder.

3. In a certain number of animals injected subcutaneously a marked hemosiderosis of the spleen was observed. There seemed to be a relationship between the degree of the splenic pigmentation and that of the local extravasations at site of injection. As such splenic pigmentation was not constant, it seems more likely that it is the result of the local hemolysis and not due to any specific action upon the blood or blood-forming organs. The splenic hemosiderosis also bore a definite relationship to the number of pigmented hemophages seen in the sinuses of the lymph and hemolymph nodes. The latter can be similarly explained. However, since hemosiderosis of the spleen is not an uncommon finding in laboratory rabbits, its occurrence in these animals may be purely coincident.

4. These changes suggest the excretion of mustard gas or some poisonous product resulting from its decomposition into the gastrointestinal tract. No positive proof, however, of this mode of excretion could be obtained. The hydrolysis of mustard gas circulating in the blood may take place in the intestinal mucosa, thereby producing the degenerative changes seen in these cells. On the other hand, the intestinal conditions may not be due to the direct action of any substance upon the epithelium of the mucosa, but may be secondary to the splanchnic congestion and the hyperexcitability of the nervous centers.

5. It seems probable that the characteristic symptoms and death following subcutaneous and intravenous injections of dichlorethylsulphide are due to the direct action of this substance circulating in the blood, upon the central nervous system, either with or without hydrolysis in the cells of the nervous tissue affected. As the result of intracellular hydrolysis, hydrochloric acid may be liberated within the cell and give rise to the toxic effects observed. The specific character and constancy of the symptomatology offer sufficient argument against any assumption that the process is embolic in character.

IV. Susceptibility

In Meyer's first laboratory experiments with dichlorethylsulphide he noticed an apparent difference in individual susceptibility, in that he, himself, was not affected by exposure to it, while a laboratory worker engaged in making it developed conjunctivitis and a severe skin eruption. Meyer's conclusion that individual susceptibility must vary greatly seems hardly warranted by this observation. Undoubtedly Meyer was working with a very impure compound, the concentration of which must have varied from time to time, and the laboratory worker must have been much more exposed to its fumes than Meyer, himself. Further, the dissemination of mustard gas is such an insidious matter of physical conditions and pure chance, that in a group of workers exposed to apparently identical conditions the greatest diversity of effects may be produced, leading to an incorrect supposition of especial resistance or susceptibility in the individual members of the same group. The question of the existence of individual susceptibility can, therefore, be settled, only by the application of experimental methods in which the conditions of exposure are identical.

This has been done by *Marshall, Lynch, Smith,* and *Williams* (Medical Division, Chemical Warfare Service Reports, Nos. 288, 290, 302, 303, 320). These workers found that the results of uniform skin tests showed that there does exist a decided individual difference in the skin reaction to mustard gas independent of changes in sensitivity due to sweating, etc. About 20-40 per cent of the white men tested showed a certain degree of resistance; while 78 per cent of negroes tested showed a similar resistance. About 2 per cent of the white individuals showed a hypersensitivity; no hypersensitive cases were found among negroes. There exists, then, a much greater degree of cutaneous sensitivity to mustard gas among white people than in the colored race. Groups of individuals treated at different times do not show any great change in sensitivity from time to time. In Report 316, *Marshall, Miller, Reed* and *Beaver* state that in the gassing chamber very little difference in susceptibilty has been noted in the dog, monkey, goat, rabbit, guinea pig, and mouse. So far as the conjunctival and respiratory mucous membrane is concerned there appears to be little or no variation in individual sensitivity. In Report 328, *Marshall* and *Williams* in a study of sensitivity in different animals in their reaction to the skin test found the horse most sensitive and monkeys most resistant, the dog most closely approaching man in percentage of reaction. Individual differences in sensitivity were also noted in animals. An acquired hypersensitivity to mustard gas vapor as the result of previous or repeated burns is claimed by many workers and accepted by some observers. That such a localized susceptibility may be shown in scars, healing burns, injured conjunctiva and mucous membranes, is very probable, and our own observations bear this out, but there is no evidence to the effect that exposures to mustard gas increase the individual's susceptibility on the part of the whole organism to this substance; but there is evidence that mustard gassing lowers the individual's resistance to tuberculosis, influenza, pneumonia, and other infections.

The individual human sensitivity is in part a racial one, and, therefore, intrinsic and constitutional. *Marshall* (Chemical Warfare Service Reports) would explain it as due to differences in the skin, cutaneous lipoids, etc. Among the individuals of the same race showing differences in cutaneous sensitivity to mustard gas he noted no other constitutional differences or peculiarities. In the cases seen by us there were five individuals who seemed to be cutaneously hypersensitive, as shown by their receiving frequent and severe burns from vapor exposures not affecting other workers so severely, although apparently similarly exposed. The two fatal cases belonged to this group. It is noteworthy that all five of these cases presented constitutional stigmata or clinical symptoms of a definite pathologic constitution, the *thymicolymphatic.*

Autopsy on one case showed a persistent thymus and characteristic lymphoid hyperplasia with exhaustion of the germ centers. The fact that individuals possessing this constitution are especially susceptible to skin conditions, such as eczema, to food idiosyncrasies, to asthma and pollen intoxications, to death from anesthesia, slight surgical operations, slight thermal burns, etc., and to death from acute infections, makes it very probable that a large number of the hypersensitive to mustard gas may possess this constitution. As its chief stigmata can be easily recognized by a good clinician, and as many of its features can be brought out by the clinical history, all workers in mustard gas should be subjected to an examination for the existence of this constitution, and those possessing it should be rejected.

The chief objective features of the constitution are a short, full neck, rounded thighs and hips, evidences of rachitis, pasty or pale complexion, tendency to mouth breathing, adenoids and enlarged tonsils, palpable lymph nodes. Occasionally these features are combined with the tuberculous habitus, long narrow flat thorax, floating ribs, long belly, low scrotum, etc.

In the clinical history the following points should be noted: tendency to croup, laryngeal stridor, asthma, hay fever, unusual tendency to bronchitis, severe reaction to acute infectious diseases, food and drug idiosyncrasies (lobster, crab, egg, honey, strawberries, raspberries, milk, cocoa, tea, morphine, chloroform, quinine, etc.), severe serum reactions, severe anaphylactic phenomena, tendency to eczematous conditions of the skin, goiter, tendency to faint on slight cause, sensitiveness to shock. At autopsy enlarged thymus and hyperplastic lymph nodes are found.

The determination of this constitution is not difficult; and an investigation should be made as to its frequency in those individuals hypersensitive to mustard gas.*

APPENDIX: Since this chapter went to press there have appeared the full articles by *Marshall* and his associates (*Journal of Pharmacology and Experimental Therapeutics*, 1918-1919). Among the points discussed is a theoretical chemical explanation of the adsorption of mustard gas on the skin. We had already shown positively that mustard gas enters the sweat glands and hair follicles, because of the deeper localization of the lesions in these structures. The uneven distribution of the lesions in the same gland would indicate that the diffusion of mustard gas into the glands is dependent upon physical conditions permitting capillary diffusion, and is not a specific chemical process.

They also state that ''Dichlorethylsulphide is absorbed through the lungs, and produces definite characteristic, systemic effects.'' We have been unable to obtain the slightest amount of evidence in support of such a view; and, as stated by us above, have never seen any characteristic systemic effects following respiratory gassing with dichlorethylsulphide. As in other forms of gassing with respiratory irritants there is a concentration of blood, with its sequelæ, but these are purely secondary to the respiratory lesions. The phenomena of shock and reflex irritations also occur; but the only characteristic systemic lesions of dichlorethylsulphide poisoning are those due to the intravenous or intradermal injections. Marshall and associates observed the same phenomena resulting from such injections, as those described above by us; and advance the same hypothesis of explanation, viz., that the dichlorethylsulphide penetrates the cells, and hydrolyzes to hydrochloric acid which is responsible for the damage. We could find no definite proof for this theory, and our attempts (in the case of rabbits) to demonstrate the excretion through the urine and intestinal tract of the hydrolyzed product of mustard gas, dihydroxyethysulphide, were entirely negative. *Marshall, Lynch and Smith,* however, state that "Dichlorethylsulphide appears to be excreted in the urine (dogs), in part at least, as dihydroxyethylsulphide." Our contradictory results leave this question still unsettled, and the hydrolysis theory of explanation of the action of mustard gas upon the cells can not be said to be demonstrated. Further, the work of *Lillie, Clowes and Chambers* (*Science,* 49, 1919) as to the action of mustard gas upon marine animals, while it supports the view of the intracellular liberation of hydrochloric acid as the toxic factor, can not be taken as a conclusive demonstration of the truth of this hypothesis. On the other hand, as we have shown above, there are good reasons for believing that the toxic action of mustard gas after intravenous and subcutaneous injections may be less simple than the hydrolysis theory would indicate.

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*Since writing the above, additional evidence of a hypersensitivity to mustard gas of individuals possessing the lymphatic constitution has been obtained in the fact that soldiers gassed with mustard gas showed a lowered resistance to influenza and pneumonia and that such susceptibility was often associated with the lymphatic constitution.

In the series of acutely fatal intravenous injections of dichlorethylsulphide described above, we noted no specific changes in blood or blood-forming organs. Since the appearance of *Pappenheimer's* preliminary report (*Society for Experimental Biology and Medicine, XVI, 92, 1919*), we have carried out a series of investigations using much smaller doses of dichlorethylsulphide in alcoholic solutions, and have been enabled to confirm Pappenheimer's observation that in rabbits living to the third or fourth day after such injections, there occurs an initial leucocytosis followed quickly by an extraordinary drop so that before death the leucocytes may practically vanish from the circulation. Two protocols are given.

Rabbit 103.—Injected intravenously with .006 c.c. of dichlorethylsulphide in alcoholic solution. A marked leucocytosis was noted in four hours. On the next day the white cells began to fall, and on the third day had reached 275. During this period the red cells remained slightly higher than normal. Blood smears showed only an occasional white cell. These were about equally divided between polynuclear leucocytes and degenerating mononuclears. Died on the fifth day.

Rabbit 104.—Given 0.010 c.c. of dichlorethylsulphide intravenously in alcoholic solution. Showed in seventeen hours a leucocytosis of 23,600. On the next day the white cells began to fall rapidly, on the fourth day reaching 325. Smears showed only occasional white cells, about equal numbers of polynuclears and degenerating mononuclears. Died on the fifth day.

Both of these animals shewed extraordinary depletion of the bone marrow and, to a lesser degree, of the spleen and lymphoid tissues. The second rabbit showed marked general edema.

Intravenous injections of small amounts of pure dichlorethylsulphide do, therefore, produce a marked leucopenia before death.

CHAPTER VI

THE CLINICAL PATHOLOGY OF MUSTARD GAS (DICHLORETHYLSULPHIDE) POISONING

By George R. Herrmann, M.S., M.D.

In the rapidly accumulating mass of literature on war gassing there are practically no reports on the clinical laboratory aspects of the condition. Even the most ordinary routine examinations as practiced daily in the smallest civilian hospital are unrecorded in the clinical reports on gassing sent from the front. Occasionally in the French reports some fragmentary laboratory observation is included. *Mandel and Gibson*,[1] speaking of the complications of mustard gas poisoning say that albuminuria is not uncommon, but that true nephritis has been rare in their experience. They comment that this is remarkable considering the frequent extensive burns of skin and mucous membranes. *Pissarello*[2] reports that in his series of sixty cases the urine was always negative to tests for sugar and albumin. If the observations on the urinary changes are few, as shown by the preceding, those on the blood changes are still more rare. *Miller*[3] has recorded observations on the blood changes found in the more or less chronic stages of gassed cases; and, although not specifically stated, some of these may have been cases of mustard gas poisoning. The exigencies of field and camp, of the field and base hospital, in the active sectors where cases of gassing would be met, have undoubtedly been such as to necessitate a sacrifice of the laboratory aspects of the condition. Further, the lack of complete laboratory facilities for the routine and special examinations, as well as of trained laboratory workers, would discourage attempts in this line of research.

Through the cooperation of Captain Lester Roos, and at the request of Doctor A. S. Warthin, an opportunity was afforded me of making observations upon the blood and urinary changes in a series of cases gassed with mustard gas. In thirty cases, we were fortunate in having a very interesting variety from the most severe types, those which resulted fatally, to those showing only the slightest lesions such as the most mild type of conjunctivitis. Nine of the severe cases, on whom the observations were fairly complete, and a tenth group of the mild cases, will be reported at this time. The latter suffered only from conjunctivitis and minor burns of the hands and fingers, and time did not permit any extensive study of this type of case. Unfortunately, our cases were not accessible until the tenth day after gassing, and then no clinical laboratory was at hand in which our work could be carried out. Further, the relative inaccessibility of the camp made the organization and maintenance of the laboratory a problem. The lack of adequate assistance during the emergency also rendered it impossible for us to do the laboratory work as completely as we had hoped. Nevertheless, we succeeded in getting a fairly complete record of the disturbances of function in the severe cases. The results determined the management and application of therapeutic measures, and the favorable effects of the instituted treatment were likewise noted. Another encouraging feature of this work is the definite and constant regularity of the results. The step-like gradation in the severity of the cases finds a parallel in the results of the various laboratory examinations; and the changes in the blood and urine show a gradual improvement, uniformly, under the adopted methods of treatment.

The Laboratory Tests and Methods Employed

The laboratory work was carried out according to the routine methods of any well-regulated hospital. Daily complete 24-hour urine specimens were collected in clean, well corked, dark glass, two liter bottles, each patient having his own bottle throughout the period in the hospital. The urine samples were examined daily. The specimen was measured and mixed in a graduated glass cylinder. The physical characteristics of the urine were noted and the reaction to red and blue litmus paper was determined. The specific gravity was taken with a urinometer graduated for work at room temperature. A sample of urine was tested for reducing substances, especially glucose, with Fehling's solution. The specimens were very carefully examined for albumin, routinely, by the Heller's fuming nitric acid ring test, and the acetic acid (8 per cent) and potassium ferrocyanide method. In many instances, and especially if there was any question as to the reaction, the heat and nitric acid, and the heat and acetic acid (3 per cent) tests, were used. The dilute ferric chloride test for the heat labile, Burgundy-red reaction of diacetic acid, as the index of acidosis, was carried out for some time in each case.

An estimate of the renal function or efficiency was obtained by the quantitative percentage determination of urea and sodium chloride, and the calculation of the daily 24-hour output of these substances, in the daily 24-hour urinary excretion.

The quantitative urine urea was determined in each case by the method of Marshall and Van Slyke in which urease, the urea splitting enzyme, obtained from the soy bean, is used to hydrolyze the urea and yield ammonia. [4, 5, 6, 7] The quantitative urine chloride estimations were made by the modified Volhard's method, in which the albumin-free urine is titrated against a solution of silver nitrate, containing 29.06 grams per liter, 1 c.c. of this solution, corresponding to 0.01 grams of sodium chloride. The ammonium thiocyanate solution used to estimate the excess of the $AgNO_3$ solution used by titration was of such a strength that 2 c.c. neutralized 1 c.c. of the silver nitrate solution. The nitric acid and iron salt indicator was used.[4, 5, 6, 7]

A few of the special examinations and tests were made on the urines. The diazo reaction of Ehrlich with sulphanilic hydrochloric acid and sodium nitrite was tried regularly for a part of the course of each case. Likewise a test for urobilinogen with paradimethylamino-benzaldehyde was carried out fairly routinely, as long as the reagent was at hand. The bromine water oxidizing method was used in the examination of the urine for melanin. Gmelin's nitric acid test and the foam test for bile pigments were employed in each case. Besides this complete chemical examination the centrifugated sediment of the urine was regularly and carefully examined microscopically.

The functional efficiency of the kidneys was further determined by estimating the percentage of phenolsulphonephthalein that was excreted, when the Rowntree and Geraghty renal functional test was applied. The quantitative estimations were made with a Dunning colorimeter. Unfortunately, the phenolsulphonephthalein and the colorimeter apparatus could not be obtained until late, that is, when the patients were convalescing.

Another index of the secretory ability of the kidney was determined by the estimation of the quantity of urea in the blood. Van Slyke's modification of Marshall's urease method was employed in this procedure as it had been in the case of the urine urea determinations. The usual enumeration of red and white blood cells, differential counting of the leucocytes and estimation of the hemoglobin were carried out. The red and white blood cells were counted in a Thoma-Zeiss hemacytometer. The hemoglobin was estimated by a Gower-Sahli hemoglobinometer and a Tallquist scale. Cover-glass blood smears were made and the preparations were stained with Wright's blood stain for differential counting. The sputum and stools were examined when indicated.

Culture media were not at hand for a complete bacteriologic examination in these cases. In the marked stage of secondary furunculosis, many smears from very young furuncles and also smears of the pus in the more mature lesions were made and stained with various staining solutions.

The Cases

The material has been arranged, and is presented, according to the severity of the cases. Beginning with Case I, the most severe, each succeeding case, in order, is less severe down through the nine cases. The seven severe cases were all gassed on the same day, June 27, but were seen for the first time by an army medical man on July 4. In Case Group No. X, all four members of which are very mild, this same order is maintained; Case X-A being the most severe of that group, and the last case practically an untouched individual, who had been with the other men, but who was apparently insusceptible to the concentrations to which the other men had reacted. The remainder of the thirty cases were similarly very mild and the laboratory examinations revealed no departures from the normal.

The blood pressure readings were not made, because the severe skin burns and especially the deep ulcerations in the bends of the elbows, made the procedure too painful in the more serious cases and it was not considered worth while in the mild ones.

The temperature, pulse and respiration tables for each case are followed by the laboratory data of the changes in the urine, blood urea and blood, with other special examinations according to the indications.

CASE I.—Patient had been severely gassed ten days before and was moribund when the blood specimen was taken. Death occurred nine hours later. Almost the entire skin surface was involved; secondary infection was marked, and a foul-smelling gangrenous layer, saturated with pus, covered the body.

TEMPERATURE, PULSE AND RESPIRATION

		T.	P.	R.
June 27	7:30 P.M.	97.6	90 (?)	20 (?)
June 28		98.5	99 (?)	20 (?)
June 29		98.8	99 (?)	20 (?)
June 30		99.8	104 (?)	20 (?)
July 1	A.M.	100.	105 (?)	20 (?)
July 2	A.M.	98.2	87 (?)	20 (?)
	P.M.	102.	152	28
July 3	6:00 A.M.		124	
	12:00 M.	100.6	110	28 (?)
	6:00 P.M.	102.8	128	28 (?)
July 4	A.M.	101.6	158	28 (?)
	P.M.	103.2	150	28 (?)
July 5	A.M.	104	140	26
	4:00 P.M.	103.6	152	26
	9:00 P.M.	104	162	28
July 6	8:00 A.M.	103	140	28
	12:00 M.	103	142	28
	4:00 P.M.	102.4	136	24
	7:45 P.M.	100	136	28
	10:15 P.M.	101	136	32
July 7	2:00 A.M.	100.2	140	28

URINE AND BLOOD UREA

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO UB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	SMITH'S TEST FOR BILE	FOAM TEST FOR BILE
July 7	60 c.c. P.M.* (Anuria**)	Acid	1020	Neg.	Pos.	Pos.	Neg.	0.13	0.18	—	—	—	—	—	—	—
7	BLOOD UREA P.M. .1104 gm. Urea per 100 c.c.															
7	COLOR OF URINE Dirty yellow. Turbid.	URINARY SEDIMENT Great showers of granular casts. Many fragmented casts. Much debris. Masses of epithelial cells (bladder and few renal). Leucocytes. Clusters of red blood cells. Amorphous urates.														

*P.M. Bladder urine postmortem.
**Patient practically had had anuria during the last twenty-four hours of life.

BLOOD

Erythrocyte count,		3,650,000
Hemoglobin,		70%
White cell count,		13,200
Differential White Count:		
Polynuclears		
Neutrophile	88%	
Eosinophile	4%	
Lymphocytes		
Large	1%	
Small	2%	
Transitionals	2%	
Myelocytes, Neutrophile	3%	

The blood platelets were not increased. The red cells show no changes. No nucleated red cells were found.

CASE II.—This was likewise a case of very severe gassing. The first blood count was made eleven days after being gassed. At that time there was a diffuse suppurative gangrenous process resulting from an extreme secondary infection of the necrosing skin. Active measures were taken to lessen the degree of the pyogenic process. The last blood count was done on the day of his death, four weeks after gassing.

TEMPERATURE, PULSE AND RESPIRATION

		T.	P.	R.
June 30		98.	72	20
July 1		100.4	105	24
July 2	A.M.	98.6	80	20
	P.M.	98.8	100	18
July 3	A.M.	100.6	112	24
	P.M.	100.8	110	20
July 4	A.M.	102.6	100	20 (?)
July 5	5:00 A.M.	102.6	158	32
	4:00 P.M.	103.6	160	32 (?)
	9:00 P.M.	103.	152	34

Temperature, Pulse and Respiration

July 6	4:00 A.M.	103.	148	32
	12:00 M.	103.	150	32 (?)
	4:00 P.M.	101.	152	28
	5:45 P.M.	103.6	152	28
July 7	4:30 A.M.	102.2	148	36
	7:00 A.M.	102.	148	38
	1:00 P.M.	102.2	140	36 (?)
	4:30 P.M.	101.6	150	36
	8:30 P.M.	102.4	152	38
	10:30 P.M.	100.	150	34
July 8	4:00 A.M.	102.6	152	36
	8:00 A.M.	103.	136	36
	1:00 P.M.	102.2	138	38
	4:00 P.M.	100.	136	36
	8:00 P.M.	103.4	140	38
July 9	4:00 A.M.	101.6	148	38
	7:30 A.M.	100.8	148	38
	12:00 M.	100.2	116	28
	4:00 P.M.	100.8	104	30
	8:00 P.M.	100.4	120	32
	12:00 P.M.	100.5	122	32 (?)
July 10	4:00 A.M.	100.6	118	30
	8:00 A.M.	100.6	128	32
	12:00 M.	100.4	120	30
	4:00 P.M.	101.	130	30
	7:45 P.M.	102.4	128	27
	12:00 P.M.	101.2	122	28
July 11	4:00 A.M.	100.8	126	25
	12:00 M.	101.	136	36
	4:00 P.M.	103.	130	32
	7:00 P.M.	101.		
	8:30 P.M.	99.	120	26
July 12	12:30 A.M.	99.4	133	28
	4:00 A.M.	99.2	120	26
	8:00 A.M.	100.8	106	30
	10:00 A.M.	101.2		
	12:00 M.	100.8	126	26
	3:00 P.M.	100.4		
	4:00 P.M.	102.3	130	34
	5:30 P.M.	100.4		
July 13	1:30 A.M.	101.	120	
	5:00 A.M.	102.4	124	
	7:00 A.M.	100.	118	22
	8:00 A.M.	101.2	120	24
	12:00 M.	102.2	126	30
	2:30 P.M.	102.2	128	30
	5:00 P.M.	103.	132	30
	8:00 P.M.	102.	130	30
	10:00 P.M.	102.	134	30
	11:15 P.M.	102.	130	
July 14	2:00 A.M.	100.6	124	28
	4:00 A.M.	100.2	126	24
	12:00 M.	101.	124	
	4:00 P.M.	102.5	140	34
	8:00 P.M.	102.	130	
	10:00 P.M.	103.	132	
	10:45 P.M.	103.5	130	
July 15	3:30 A.M.	101.	126	24
	7:00 A.M.	100.5	118	24
	12:00 M.	103.6	134	30
	4:00 P.M.	102.5	140	34
	8:30 P.M.	102.2	125	
	9:00 P.M.	103.2	126	

Temperature, Pulse and Respiration

July 15	12:00 P.M.	102.2	97	
July 16	1:00 A.M.	101.2	100	
	4:00 A.M.	101.6	115	
	5:00 A.M.	101.8	119	
	7:00 A.M.	100.	121	
	8:00 A.M.	106.6	128	34
	12:00 M.	101.	116	32
	4:00 P.M.	102.2	110	
	8:00 P.M.	103.	120	
	10:00 P.M.	99.8	124	
	10:30 P.M.	99.8	125	
	11:00 P.M.		110	
	11:30 P.M.		120	
	12:00 P.M.	102.	115	
July 17	12:30 A.M.			
	2:30 A.M.	102.6	116	
	4:00 A.M.	101.2	115	
	5:00 A.M.	101.2	126	
	6:00 A.M.	99.2	126	
	8:00 A.M.	100.6	120	30
	12:00 M.	100.4	112	28
	4:00 P.M.	100.4	128	28
	8:00 P.M.	101.8	125	
	10:00 P.M.	99.8	120	
	12:00 P.M.	101.	120	
July 18	2:00 A.M.	98.8	115	
	4:00 A.M.	98.8	120	
	8:00 A.M.	100.	126	32
	1:00 P.M.	100.4	116	28
	5:00 P.M.	100.6	128	
	8:00 P.M.	101.8	120	
	12:00 P.M.	102.	130	
July 19	4:00 A.M.	100.2	124	28
	8:00 A.M.	100.	128	28
	1:00 P.M.	100.6	120	28
	4:00 P.M.	101.4	120	28
	8:00 P.M.	101.6	120	
	12:00 P.M.	101.6	120	28
July 20	4:00 A.M.	101.4	125	
	4:30 A.M.	100.2		
	8:00 A.M.	99.8	120	30
	12:00 M.	100.2	124	32
	4:00 P.M.	101.4	124	34
	8:00 P.M.	102.2	120	
	10:00 P.M.	101.2	124	
	12:00 P.M.	101.2	125	
July 21	4:00 A.M.	101.4	120	
	6:00 A.M.	99.8	105	
July 21	8:00 A.M.	99.8	124	30
	12:00 M.	101.2	124	30
	4:00 P.M.	101.6	128	32
	8:00 P.M.	102.4	130	
	10:00 P.M.	100.	120	
	12:00 P.M.	101.6	122	
July 22	2:00 A.M.	100.2	124	
	4:00 A.M.	101.2	126	
	6:00 A.M.	98.6	120	
	8:00 A.M.	99.6	130	
	11:00 A.M.		136	50
	12:00 M.	101.6	140	50
	4:00 P.M.	102.	152	52
	5:00 P.M.		160	58

URINE AND BLOOD UREA

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.									gm.	gm.					
8	1850	Acid	1018	Neg.	Pos.?	Pos.?	Neg.	—	0.16	—	2.96	—	—	—	Neg.	Neg.
9	1470	"	1024	Neg.	Pos.	Pos.	Neg.	—	0.24	—	3.53	—	—	—	Neg.	Neg.
10	1000	"	1020	Neg.	Pos.	Pos.	Neg	0.53	0.10	5.30	1.00	—	—	—	Neg.	Neg.
11	1650	"	1012	Neg.	Pos.	Pos.	Neg.	—	0.22	—	3.33	Neg.	—	Neg.	Neg.	Neg.
12	1150	"	1013	Neg.	Pos.	Pos.	Neg.	0.74	0.40	8.51	4.60	Neg.	—	Neg.	Neg.	Neg.
13	1200	"	1015	Neg.	Pos.?	Pos.	Neg.	0.38	—	4.56	—	Neg.	—	Neg.	Neg.	Neg.
14	2000	"	1011	Neg.	Pos.	Pos.	Neg.	1.80	—	36.0	—	Neg.	—	Neg.	Neg.	Neg.
15	—*	"	1015	Neg.	Pos.	Pos.	Neg.	1.35	—	—	—	Neg.	—	Neg.	Neg.	Neg.
16	1550	"	1013	Neg.	Pos.	Pos.	Neg.	0.54	0.30	8.37	4.65	Neg.	Pos.	Neg.	Neg.	Neg.
17	500*	"	1024	Neg.	Trace	Trace	Neg.	—	0.50	—	2.50	—	Pos.	—	Neg.	Neg.
18	730*	"	1020	Neg.	"	"	Neg.	0.84	0.52	6.16	3.79	—	Pos.	—	Neg.	Neg.
19	750*	"	1015	Neg.	"	"	Neg.	0.54	0.66	4.05	4.95	—	Neg.	—	Neg.	Neg.
20	800*	"	1013	Neg.	Neg.	Neg.	Neg.	—	0.44	—	3.52	—	—	—	—	—
21	1075*	"	1007	Neg.	Trace	Trace	Neg.	0.35	0.54	3.76	5.80	—	—	—	—	—
22	1475*	"	1008	Neg.	"	"	Neg.	—	0.42	—	6.19	—	—	—	—	—

	BLOOD UREA
10	.036 Gm. per 100 c.c.

	COLOR OF URINE	URINARY SEDIMENT
8	Deep red brown.	Amorphous urates. Few granular casts. Bladder and kidney epithelial cells. Many leucocytes. Few red blood cells.
11	Brownish yellow.	Amorphous urates. Granular casts. Leucocytes. Epithelial cells, plus the sediment of some alkaline fermentation—triple phosphates especially.
13	Dark brown.	Excess of uric acid crystals. Amorphous urates. Large number of red blood cells. Few granular casts and epithelial cells.
15	"	Incontinence, no specimen collected.
16	Amber	Much improved. Amorphous urates. Leucocytes. Few fragmented granular casts. Epithelial cells. Few bacteria (contamination). No red blood cells.
17	Dark amber.	Few amorphous urates. Few leucocytes. Few granular and epithelial cells. Bacteria.
18	"	Excessive amount of uric acid and amorphous urates coloring the sediment bright red. Few leucocytes. Few granular casts. Few renal epithelial cells.
19	Light amber.	Sediment is much improved. Few amorphous urates. Few granular epithelial cells. Few leucocytes. One or two hyaline casts.
20	Amber.	Apparently much improved. Few amorphous urates. Leucocytes, and granular epithelial cells.
21	"	Abundant urates. Few hyaline and fragmented granular casts. Few granular epithelial cells. Few leucocytes.
22	"	Large amount of amorphous urates. Many uric acid crystals. Numerous hyaline casts and renal epithelial cells. Few red and white blood cells.

*Incontinence.

BLOOD

	ERYTHROCYTE COUNT	WHITE COUNT	HEMOGLOBIN
July 8	4,100,000	29,700	75%
July 11	4,250,000	21,500	80%
July 14	....	13,000	....
July 15	....	13,500	....
July 18	....	13,000	....
July 20	....	12,700	65%
July 22	....	10,800	....

Differential white count on July 11, 11 days after gassing.

Polynuclears	
Neutrophile	86.5 %
Eosinophile	6.75%
Basophile	.5 %
Degenerates	.75%
Lymphocytes	
Large	.25%
Small	.75%
Transitionals	.5 %
Large basophilic mononuclears	1.0 %
Myelocytes	
Neutrophile	2.5 %
Eosinophile	.25%
Myeloblasts	.25%

The polymorphonuclears are chiefly young types, showing the Arneth scale to the left. The eosinophilia is marked. The blood platelets are large and numerous. One megaloblast was found in counting four hundred white cells. No other changes in the red cells were noted.

CASE III.—This patient was very severely gassed. He early developed a severe secondary infection with diffuse suppuration. There was also an extensive bronchopneumonia. After institution of active treatment by irrigation and continuous baths, the pyogenic process rapidly cleared up. Recovery after two months. The first blood count was made two weeks after gassing, and the last, four weeks after gassing.

TEMPERATURE, PULSE AND RESPIRATION

		T.	P.	R.
June 28	A.M.	99.4	90	28
	P.M.	99.8	100	30
June 29	A.M.	100.	110	28
	P.M.	100.	110	28
June 30	A.M.	99.8	109	28 (?)
	P.M.	97.	104	28
July 1	A.M.			
	P.M.	100.8	108	26
July 2	A.M.	99.2	105	28
	P.M.	100.8	108	26
July 3	A.M.	101.	108	26
July 4	A.M.	99.6	109	18
July 5	4:00 A.M.	103.4	128	28
	4:00 P.M.	102.6	128	24
	9:00 P.M.	103.	132	30
July 6	4:00 A.M.	102.	132	26
	12:00 M.	102.	128	32
	4:00 P.M.	103.	132	28
	10:00 P.M.	102.4	120	24
July 7	2:00 A.M.	102.2	128	26
	6:30 A.M.	102.6	128	26
	12:00 M.	103.4	132	28
	4:30 P.M.	103.4	130	28
	10:30 P.M.	102.8	132	28
July 8	2:00 A.M.			
	4:00 A.M.	100.4	126	28
	8:00 A.M.	100.4	114	28
	12:00 M.	102.2	120	28
	4:00 P.M.	101.6	126	32
	8:00 P.M.	102.	132	32

Temperature, Pulse and Respiration

July 8	12:00 P.M.	102.2	132	28
July 9	5:00 A.M.	101.	130	28
	8:00 A.M.	99.8	120	26
	12:00 M.	102.	136	32
	4:00 P.M.	101.4	120	34
	8:00 P.M.	101.8	130	34 (?)
	12:00 P.M.	99.8	127	34 (?)
July 10	4:30 A.M.	100.6	132	34
	8:00 A.M.	101.6	130	32
	12:00 M.	100.4	128	30
	4:00 P.M.	100.4	124	26
	8:00 P.M.	100.4	118	24
July 11	1:00 A.M.	101.	120	24
	4:00 A.M.	99.2	119	24
	12:00 M.	100.	128	32
	4:00 P.M.	100.6	140	34
	8:00 P.M.	100.8		
	12:00 P.M.	99.4	120	22
July 12	4:00 A.M.	99.6	120	19
	8:00 A.M.	99.8	126	20
	12:00 M.	100.6	120	36
	4:00 P.M.	101.2	124	34
	8:00 P.M.	102.	124	33
	10:00 P.M.	99.4	118	22
July 13	12:30 A.M.	99.2	118	22
	5:00 A.M.	99.3	124	20
	12:00 M.	100.6	136	32
	1:00 P.M.	101.	134	30
	4:00 P.M.	101.	124	28
	8:00 P.M.	100.8	125	
July 14	1:00 A.M.	100.4	120	
	4:00 A.M.	100.	124	20
	8:00 A.M.	101.2	130	26
	3:00 P.M.	102.2	128	20
	4:00 P.M.	101.4	130	30
	8:00 P.M.	100.8	120	
	11:30 P.M.	100.6	118	22
July 15	4:00 A.M.	100.6	118	22
	8:00 A.M.	101.5	128	32
	12:00 M.	102.2	136	30
	4:00 P.M.	102.2	128	28
	8:00 P.M.	101.	125	28
July 16	12:30 A.M.	101.	129	31
	5:30 A.M.	100.8	125	27
	8:00 A.M.	100.6	136	28
	12:00 M.	100.4	124	32
	4:00 P.M.	101.	126	28
	8:00 P.M.	101.8	129	28
July 17	1:00 A.M.	100.	130	26
	5:00 A.M.	100.	132	32
	8:00 A.M.	101.	128	30
	12:00 M.	101.	130	28
	4:00 P.M.	101.6	128	28
	8:00 P.M.	101.	128	28
	12:00 P.M.	100.4	127	28
July 18	4:00 A.M.	99.	126	27
	8:00 A.M.	100.8	130	30
	1:00 P.M.	101.3	126	28
	8:00 P.M.	101.2	130	28
	12:00 P.M.	100.	134	36
July 19	4:00 A.M.	99.8	130	32

Temperature, Pulse and Respiration

July 19	8:00 A.M.	101.2	126	28
	12:00 M.	100.6	120	26
	4:00 P.M.	101.5	128	28
	8:30 P.M.	102.2	130	31
	11:00 P.M.	101.2	124	29
July 20	1:00 A.M.	101.4	124	28
	1:45 A.M.	100.	122	30
	6:00 A.M.	100.4	124	26
	8:00 A.M.	100.6	120	22
	12:00 M.	99.8	120	20
	4:00 P.M.	101.6	128	26
	8:00 P.M.	101.8	88	24
	12:00 P.M.	100.6	128	26
July 21	4:00 A.M.	100.	128	24
	8:00 A.M.	99.8	116	22
	12:00 M.	100.6	120	26
	4:00 P.M.	101.3	124	22
	8:00 P.M.	100.8	124	24
	12:00 P.M.	100.	120	20
July 22	4:00 A.M.	100.	122	24
	8:00 A.M.	100.	120	22
	12:00 M.	100.	112	24
	4:00 P.M.	100.4	120	26
	8:00 P.M.	100.2	114	24
	12:00 P.M.	99.4	118	28
July 23	4:00 A.M.	98.3	120	26
	8:00 A.M.	100.2	116	24
	12:00 M.	99.8	124	24
	4:00 P.M.	100.	112	22
	8:00 P.M.	99.	116	30
	12:00 P.M.	99.6	120	30
July 24	4:00 A.M.	99.6	120	28
	8:00 A.M.	99.8	112	26
	12:00 M.	99.6	116	26
	4:00 P.M.	99.8	120	24
	8:00 P.M.	99.6	112	28
	12:00 P.M.	99.4	118	28
July 25	4:00 A.M.	99.8	124	22
	8:00 A.M.	101.4	124	24
	10:00 A.M.	101.8	128	24
	12:00 M.	102.	124	24
	4:00 P.M.	100.6	120	24
	8:00 P.M.	100.	120	24
	12:00 P.M.	99.6	118	24
July 26	4:00 A.M.	99.2	130	26
	8:00 A.M.	99.4	116	26
	12:00 M.	99.4	114	28
	4:00 P.M.	99.8	118	28
	8:00 P.M.	99.4	120	26
	12:00 P.M.	99.	110	22
July 27	4:00 A.M.	99.	120	22
	8:00 A.M.	99.	116	28
	12:00 M.	99.2	120	24
	4:00 P.M.	99.6	114	24
	8:00 P.M.	99.4	116	26
	12:00 P.M.	99.2	118	26
July 28	4:00 A.M.	98.6	120	20
	8:00 A.M.	99.	108	22
	12:00 M	99.4	116	26
	4:00 P.M.	99.8	110	24
	8:00 P.M.	99.4	120	20

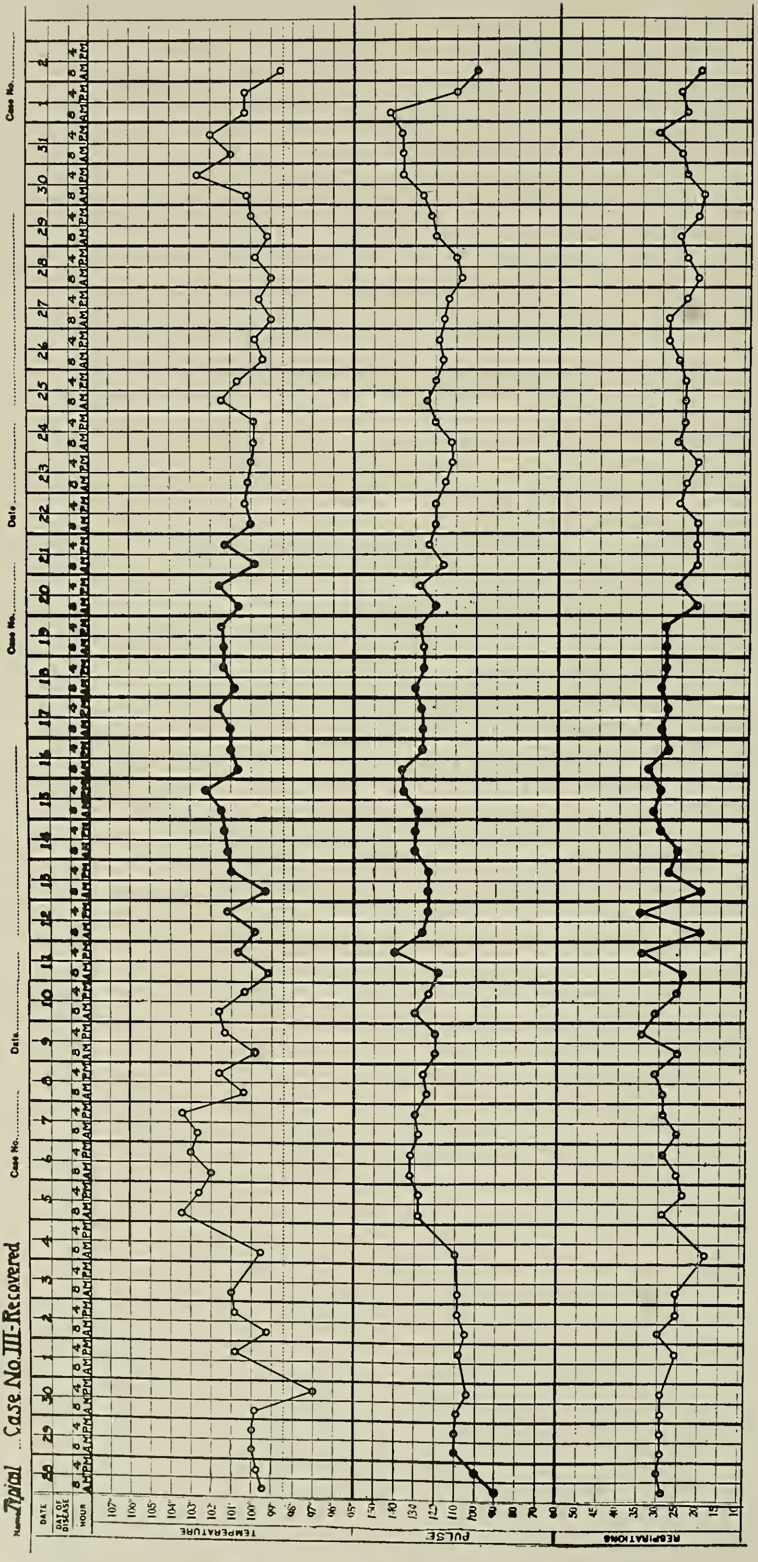
Name Typical Case No. III-Recovered
Case No.
Date
DATE
DAY OF DISEASE
HOUR
8 4 AM PM
28 29 30 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 1 2
TEMPERATURE
107° 106° 105° 104° 103° 102° 101° 100° 99° 98° 97° 96° 95°
PULSE
150 140 130 120 110 100 90 80 70 60
RESPIRATIONS
50 45 40 35 30 25 20 15 10

Chart I.

Temperature, Pulse and Respiration

July 28	12:00 P.M.	99.4	116	22
July 29	4:00 A.M.	99.4	122	26
	8:00 A.M.	99.2	120	26
	12:00 M.	99.6	114	24
	8:00 P.M.	100.	122	22
	12:00 P.M.	100.4	124	26
July 30	4:00 A.M.	99.4	116	22
	8:00 A.M.	100.2	126	20
	12:00 M.	101.6	132	24
	4:00 P.M.	102.6	136	24
	8:00 P.M.	101.8	136	28
	12:00 P.M.	100.4	136	28
July 31	4:00 A.M.	100.4	136	28
	8:00 A.M.	101.	136	26
	12:00 M.	101.6	130	32
	4:00 P.M.	102.	136	32
	7:00 P.M.	101.8	136	26
	8:00 P.M.	101.6	138	26
Aug. 1	12:00 P.M.	100.2	120	24
	4:00 A.M.	100.2	136	30
	8:00 A.M.	100.2	132	24
	12:00 M.	100.	118	22
	4:00 P.M.	100.2	110	26
	8:00 P.M.	99.6	110	24
	12:00 P.M.	98.6	100	22
Aug. 2	4:00 A.M.	98.6	100	24
	6:00 A.M.	98.6	100	26
	8:00 A.M.	98.6	100	22

(For graphic chart of temperature, pulse and respiration see Chart I.)

The further recovery was uneventful. The patient was discharged as completely cured about a month later.

Blood

	ERYTHROCYTE COUNT	WHITE COUNT	HEMOGLOBIN
July 10	4,650,000	24,600	75%
July 12	4,800,000	21,500	75%
July 14	....	20,000	75%
July 16	....	15,000	....
July 18	....	15,000	....
July 20	....	16,000	....
July 22	....	15,700	....
July 24	....	15,400	....
July 26	....	15,500	....

Differential white counts two weeks, and four weeks after gassing.

	July 11	July 25
Polynuclears		
Neutrophile	86%	79.5%
Eosinophile	7%	2.0%
Basophiles	....	1.5%
Lymphocytes		
Large	....	1.0%
Small	1%	8.5%
Transitionals	....	.5%
Large basophilic mononuclears	2%	3.5%
Myelocytes, neutrophilic.	4%	3.5%

The platelets were increased, particularly in the earlier smears. There is an increase in the large deeply staining mononuclears. The red cells show no change and no nucleated red cells were found.

PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE					SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	FLUID INTAKE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO$_3$ RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July		c.c.									gm.	gm.					
8		1275	Acid	1025	Neg.	Pos.	Pos.	Neg.	—	0.06	—	0.765	—	—	—	Neg.	Neg.
9		1170	"	1025	Neg.	Pos.	Pos.	Neg.	—	0.48	—	5.6	—	—	—	Neg.	Neg.
10		1000	"	1025	Neg.	Pos.	Pos.	Neg.	0.40	0.10	4.00	1.0	—	—	—	Neg.	Neg.
11		1050	"	1017	Neg.	Pos.	Pos.	Neg.	—	0.10	—	1.05	Neg.	—	Neg.	Neg.	Neg.
FLUIDS FORCED																	
12		1870	"	1015	Neg.	Pos.	—	Neg.	0.59	0.06	—	1.12	Neg.	—	Neg.	Neg.	Neg.
13		1950	"	1014	Neg.	Pos.	—	Neg.	0.40	—	7.8	—	Neg.	—	—	Neg.	Neg.
14		1700	Slight	1017	Neg.	Pos.	—	Neg.	1.75	—	29.57	—	Neg.	Pos.	—	Neg.	Neg.
15			Acid	1015	Neg	Pos.	—	Neg.	1.42	0.12	—	—	—	Pos.	—	Neg.	Neg.
16		550	"	1020	—	Pos.	—	—	0.52	0.12	—	—	—	Pos.	—	Neg.	Neg.
17		850	"	1027	—	Pos.	—	—	0.31	0.08	2.63	0.68	—	Pos.	—	Neg.	Neg.
18	3300	750	"	1027	—	Pos.	—	—	0.88	0.10	6.6	0.75	—	Pos.	—	Neg.	Neg.
19	2640	800	"	1025	—	Pos.	—	—	0.58	0.36	4.6	2.88	—	Pos.	—	Neg	Neg.
20	3660	1400	"	1013	—	Pos.	—	—	—	0.20	—	2.80	—	Neg.	—	Neg.	Neg.
21	2640	1925	"	1009	—	Pos.	—	—	0.44	0.22	8.47	4.24	—	Neg.	—	Neg.	Neg.
22	3360	1650	"	1013	—	Pos.	—	—	—	.0.26	—	4.29	—	Pos.	—	Neg.	Neg.
23	3360	1530	Ampho teric	1010	—	Trace	—	—	—	0.70	—	10.71	—	Neg.	—	Neg.	Neg.
24	2880	950	"	1022	—	Trace	—	—	—	0.80	—	7.6	—	—	—	—	—
25	2880	1750	"	1010	—	Trace	—	—	—	0.48	—	8.4	—	—	—	—	—
26	2640	2450	Neutral	1010	—	Trace	—	—	0.94	0.30	23.00	7.35	—	—	—	—	—
27	2160	2200	Slt. Ac.	1008	—	Trace	—	—	0.48	0.26	10.56	6.72	—	—	—	—	—
28	1920	1600	" "	1015	—	Neg.	Neg.	—	0.60	0.30			—	—	—	—	—
29	1920	2100	Neutral	1015	—	Neg.	Neg.	—	0.52	—	10.92	—	—	—	—	—	—
30	—	—	Slt. Ac.	1015	—	Trace	Trace	—	—	0.55	—	—	—	—	—	—	—
31	—	1900	" "	1012	—	Neg.	Neg.	—	—	—	—	—	—	—	—	—	—

BLOOD UREA

7/10 .060 Gm. per 100 c.c. blood.
28 .045 " " " " "

PHENOLSULPHONEPHTHALEIN

7/24 1st hr. plus 10 min. 1:00 to 2:10 50%
2nd hr. 2:10 to 3:10 No specimen obtainable.
Total.................... 50%
At 3:30 15%

SPUTUM

Mucopurulent, frothy, profuse in amount. More than usual number of streptococci, in chains of medium length.

CAST OF BRONCHUS

Pink flesh-like. Smears showed practically a mixed culture of rather medium short chained streptococci, Gram positive diplococci, and Gram negative large thick bacilli in chains.

	COLOR OF URINE	URINARY SEDIMENT
8	Transparent, red brown.	Very heavy shower of granular casts and peculiar split fiber casts. Leucocytes. Few red blood cells. Amorphous urates. Epithelial cells.
9	Translucent, red, yellow.	
10	Lighter	
11	Darker again.	Amorphous urates, granular casts, leucocytes and red blood cells.
FLUIDS FORCED		
12	Medium dark.	Excess amorphous urates. Uric acid. Few granular casts. Mucous cylindroids. Red blood cells.
13	" "	
14	Dark.	
15	"	
16	"	Somewhat improved. Amorphous urates. Leucocytes. Few hyaline and granular casts; renal and bladder epithelial cells.
17	"	Amorphous urates. Leucocytes, hyaline and fragments of granular casts. Red blood cells. Calcium oxalate crystals.
18	"	Abundant amorphous urates. Uric acid. Red and white blood cells. Few granular casts and epithelial cells.
19	Muddy.	Much improved. Few granular casts and epithelial cells. Few leucocytes. Bacteria.
20	Lighter.	Still improving. Amorphous urates. Few granular casts. Epithelial cells. Alkaline fermentation sediment with triple phosphates.
21	Slightly dark.	Abundant amorphous urates. Few red and white blood cells. Few granular casts and epithelial cells.
22	Darker.	Large amounts of sediment. Amorphous urates, granular epithelial cells. Few triple phosphates.
23	Lighter.	Amorphous urates. Few granular casts. Epithelial cells. Triple phosphates.
24	Normal.	Amorphous urates. Triple phosphates. Few granular epithelial cells.

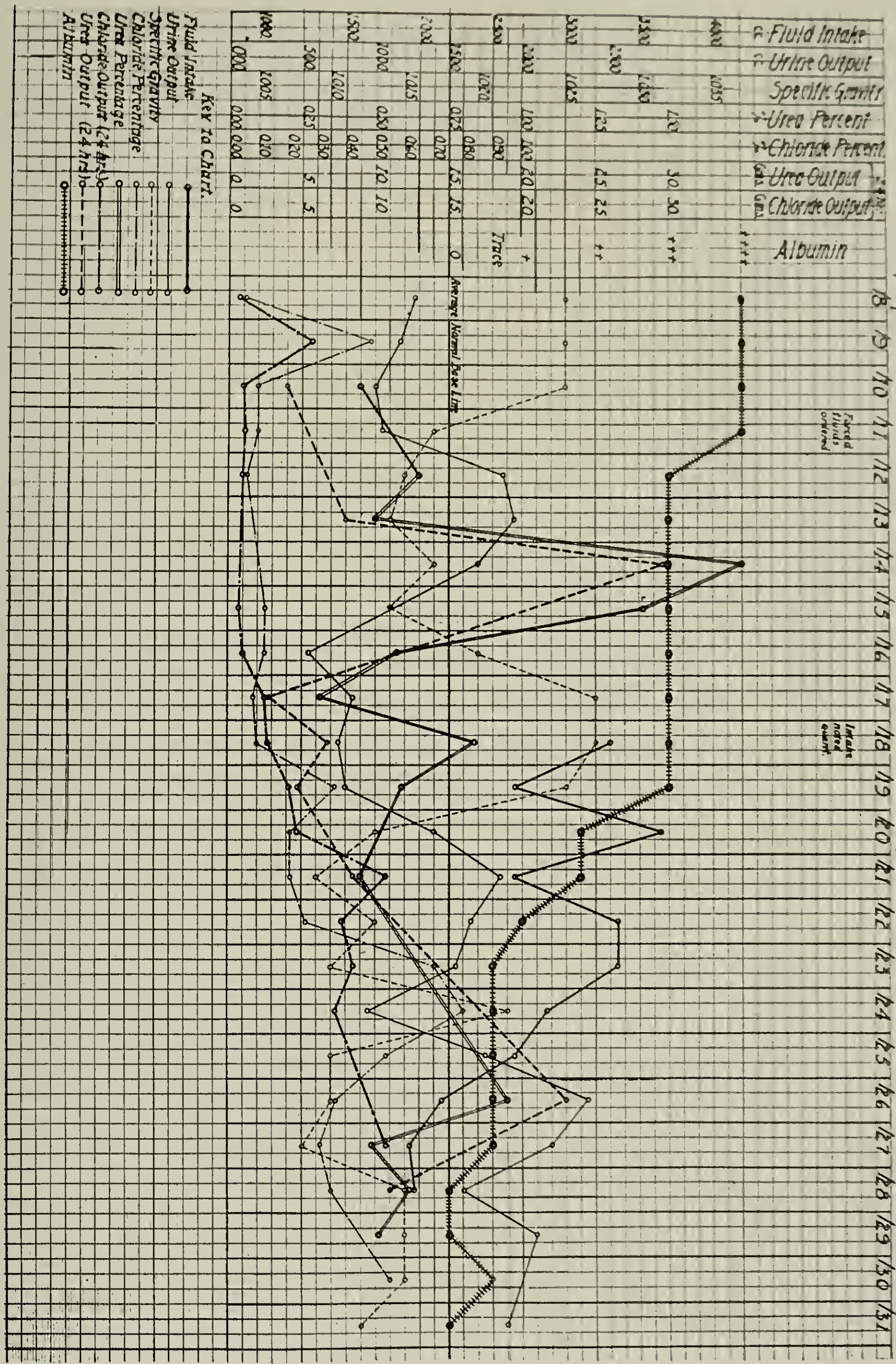
Graphic Chart of Urine Laboratory Data - Typical Case No. III.
Fluid Intake
Urine Output
Specific Gravity
Urea Percent
Chloride Percent
Urea Output
Chloride Output
Albumin
Key to Chart.
Fluid Intake
Urine Output
Specific Gravity
Chloride Percentage
Urea Percentage
Chloride Output (24 hrs)
Urea Output (24 hrs)
Albumin
Average Normal Base Line
Forced fluids ordered
Intake noted exact.
Trace
1/8
1/9
1/10
1/11
1/12
1/13
1/14
1/15
1/16
1/17
1/18
1/19
1/20
1/21
1/22
1/23
1/24
1/25
1/26
1/27
1/28
1/29
1/30
1/31

Chart II.

	COLOR	SEDIMENT
25	Slightly dark.	Amorphous urates. Uric acid. Triple phosphates. Few granular leucocytes and epithelial cells.
26	Normal.	Slight sediment. Alkaline fermentation. Triple phosphates.
27	Medium dark.	Amorphous urates and triple phosphates.
28	Normal.	Amorphous urates and triple phosphates.
29	"	Much sediment, carbonates.
30	Sl. darker.	Few amorphous urates and triple phosphates. Few granular epithelial cells.
31	Normal.	Few granular epithelial cells, few leucocytes, otherwise normal.

(For graphic chart of the urinary changes, see Chart II.)

Case IV.—This was a rather severe case of mustard gassing. The patient had extreme nausea and vomiting for five hours during the first night after being gassed. He developed severe genital lesions which became secondarily infected. There was also necrosis of the nasal and pharyngeal mucosa and some bronchitis.

Temperature, Pulse and Respiration

		T.	P.	R.
July 4		Normal	Normal	Normal
July 5	8:00 A.M.	98.6	96	26
	4:00 P.M.	98.2	80	
July 6	4:00 A.M.	97.	80	18
	4:00 P.M.	98.6	96	18
July 7	6:00 A.M.	97.4	82	19
	4:30 P.M.	99.	100	22
July 8	8:00 A.M.	97.4	92	22
	4:00 P.M.	97.6	94	22
July 9	4:00 P.M.	98.6	102	20
July 10	8:00 A.M.	97.6	100	24
	4:00 P.M.	98.6	98	20
July 11	4:00 P.M.	99.	112	24
July 12	4:00 P.M.	99.6	106	22
July 13	4:00 P.M.	100.	116	22
July 14	4:00 P.M.	100.	109	
July 15	8:00 A.M.	98.8	112	18
	4:00 P.M.	99.8	112	28
July 16	8:00 A.M.	98.8	86	
	4:00 P.M.	98.8	92	
July 17	7:30 A.M.	98.2	98	
	4:00 P.M.	98.8	78	
July 18	7:30 A.M.	100.	98	
	4:00 P.M.	99.8	88	
July 19	8:00 A.M.	98.8	80	
	4:00 P.M.	98.8	88	
July 20	7:30 A.M.	98.6	86	
	4:00 P.M.	99.	88	
July 21	7:30 A.M.	98.4	82	
	4:00 P.M.	99.	76	
July 22	7:30 A.M.	98.2	78	
	4:00 P.M.	98.8	82	
July 23	8:00 A.M.	98.6	78	20
	4:00 P.M.	98.6	98	20
July 24	8:00 A.M.	98.	80	18
	4:00 P.M.	98.6	112	20
July 25	8:00 A.M.	98.6	86	
	4:00 P.M.	98.8	88	
July 26	8:00 A.M.	98.6	80	
	4:00 P.M.	98.8	84	
July 27	8:00 A.M.	98.4	82	
	4:00 P.M.	98.6	86	
July 28	8:00 A.M.	98.	84	20
	4:00 P.M.	98.6	98	22
July 29	8:00 A.M.	98.2	86	18
	4:00 P.M.	98.6	98	

URINE AND BLOOD UREA

PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE				SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.									gm.	gm.					
8	1000	Acid	1026	Neg.	Pos.	Pos.	Neg.	—	0.14	—	1.40	—	—	—	Neg.	Neg.
9	1000	"	1030	Neg.	Pos.	Pos.	Neg.	—	0.20	—	2.00	—	—	—	Neg.	Neg.
10	1600	"	1018	Neg.	Pos.	Pos.	Neg.	0.36	0.32	5.76	5.12	—	—	—	Neg.	Neg.
11	525	"	1023	Neg.	Pos.	Pos.	Neg.	—	0.26	—	1.36	Neg.	—	Neg.	Neg.	Neg.
12	1025	"	1020	Neg.	Pos.		Neg.	0.68	0.26	6.97	2.67	Neg.	—	Neg.	Neg.	Neg.
13	1600	"	1013	Neg.	Pos.		Neg.	0.62	—	9.92	—	Neg.	—	—	Neg.	Neg.
14	1100	Amphoteric	1027	Neg.	Pos.		Neg.	2.56	—	28.16	—	Neg.	—	Neg.	Neg.	Neg.
15		Neutral	1015	—	Pos.		Neg.	1.22	0.20	—	—	—	Neg.	—	Neg.	Neg.
16	No specimen collected.															
17	350	Acid	1023	—	Pos.		Neg.	—	0.30	—	1.05	—	Neg.	—	Neg.	Neg.
18	1150	Neutral	1015	—	Pos.		—	0.67	0.80	7.60	9.20	—	Neg.	—	Neg.	Neg.
19	450?	Acid	1020	—	Neg.	Neg.	—	0.24	0.60	1.08	2.70	—	Neg.	—	Neg.	Neg.
20	650	"	1017	—	Neg.	Neg.	—	—	0.26	—	1.69					
21	540	"	1022	—	Pos.	Pos.	—	—	0.60	—	3.24	—	Neg.	—	Neg.	Neg.
22	1100	"	1019	—	Pos.	Pos.	—	—	0.58	—	6.38	—	Neg.	—	Neg.	Neg.
23	1075	Slight	1015	—	Neg.	Neg.	—	—	0.48	—	5.16	—	—	—	—	—
24	1000	"	1022	—	Neg.	Neg.	—	—	0.50	—	5.00	—	—	—	—	—
25	625	"	1017	—	Neg.	Neg.	—	—	0.58	—	3.62	—	—	—	—	—
26	1200	"	1022	—	Neg.	Neg.	—	1.05	0.58	1.80	6.96	—	—	—	—	—
27	800	"	1025	—	Pos.	Pos.	—	0.74	0.46	5.92	3.68	—	—	—	—	—
28	300	"	1023	—	Neg.	Neg.	—	0.72	0.66	2.16	1.98	—	—	—	—	—
29	500	"	1022	—	Neg.	Neg.	—	0.52	—	2.60	—	—	—	—	—	—

BLOOD UREA	PHENOLSULPHONEPHTHALEIN TEST
10 .0480 gm. per 100 c.c.	July 24 1st hr. plus 10 min. 9:30 to 10:40 — 80% 2nd hr. 10:40 to 11:40 — 10% Total............90%

	COLOR OF URINE	URINARY SEDIMENT
8	Medium lemon yellow. Turbid, heavy deposit.	Uric acid. Amorphous urates, crystals in showers. Cylindroids. Few granular casts. Epithelial cells.
9	Medium yellow, translucent.	
10	Straw color. Slightly turbid.	
11	Darker. Turbid.	Uric acid and amorphous urates in great showers. Few granular casts. Few white and red blood cells, few epithelial cells.
12	Normal.	Uric acid and amorphous urates. Otherwise negative.
13	Turbid.	
14	Dirty yellow.	
15	Normal.	
16	NO SPECIMEN COLLECTED	
17	Medium dark, turbid.	Few uric acid and amorphous urates. Few triple phosphates and calcium oxalate. Few hyaline casts, renal and urethral epithelial cells. Numerous leucocytes.
18	Slightly dark, translucent.	Abundant uric acid and urates. Few triple phosphates, few granular epithelial casts.
19	Normal sediment.	Almost entirely amorphous urates. Few uric acid and few triple phosphates.
20	Normal.	Abundant amorphous urates, few uric acid, triple phosphates. Granular casts and granular epithelium.
21	Normal.	As above.
22	Normal.	As above but no casts noted.
23	Somewhat pale.	As above but no casts noted.
24	Normal.	As above but no casts noted.
25	Normal.	As above but no casts noted.
26	Normal.	Only triple phosphates and a few epithelial cells.
27	Medium dark.	As above.
28	Normal.	As above.
29	Normal.	Amorphous urates. Uric acid. Numerous leucocytes. Triple phosphates.

BLOOD

Examination of blood two weeks after gassing.

Erythrocyte count		4,500,000
White count		25,000
Hemoglobin		76%
Differential white count:		
Polynuclears		
Neutrophile	84.0%	
Eosinophile	1.5%	
Lymphocytes		
Large	2.0%	
Small	3.0%	
Transitionals	.5%	
Large basophilic mononuclears	1.5%	
Myelocytes, neutrophilic,	7.5%	

The blood platelets were increased. There were no changes in the red cells.

CASE V.—This patient had severe mustard gas burns about the genitals, in the axillæ and at the bends of the elbows. There was a less severe generalized burn. A marked generalized secondary furunculosis complicated the later course of this patient.

TEMPERATURE, PULSE AND RESPIRATION

		T.	P.	R.
June 27	7:30 P.M.	97.6	112	26
June 28		98.2	110	24
June 30		98.6	90	
July 1		99.	82	
July 2		98.8	90	
July 3	5:00 P.M.	98.8	97	
July 4	6:00 A.M.	98.4	110	
July 5	4:00 P.M.	100.	108	
July 6	4:00 A.M.	98.	102	22
	4:00 P.M.	99.2	116	22
July 7	4:00 A.M.	98.	108	22
	4:00 P.M.	98.6	104	22
July 8	2:45 A.M.			
	4:00 A.M.	97.	110	
	4:00 P.M.	99.6	112	18
July 9	4:00 A.M.	98.8	98	20
July 10	8:00 A.M.	96.8	112	16
	4:00 P.M.	99.4	112	24
July 11	4:00 P.M.	99.	110	22
July 12	4:00 P.M.	99.4	106	22
July 13	4:00 P.M.	100.6	102	20
July 14	7:30 P.M.	102.	110	
July 15	8:00 A.M.	99.	100	18
	12:00 M.	98.8	100	18
	4:00 P.M.	100.	112	26
July 16	8:00 A.M.	98.6	88	
	4:00 P.M.	98.6	92	
July 17	7:30 A.M.	98.2	88	
	4:00 P.M.	98.	82	
July 18	7:30 A.M.	98.2	88	
	4:00 P.M.	98.2	84	
July 19	8:00 A.M.	97.8	80	
	4:00 P.M.	98.	78	
July 20	7:30 A.M.	97.6	68	
	4:00 P.M.	98.4	76	
July 21	8:00 A.M.			
	4:00 P.M.	98.8	78	

Temperature, Pulse and Respiration

July 22	7:30 A.M.	97.8	76	
	4:00 P.M.	98.6	80	
July 23	8:00 A.M.	98.	68	
	4:00 P.M.	98.2	76	
July 24	8:00 A.M.	97.	74	
	4:00 P.M.	98.6	82	
July 25	8:00 A.M.	97.6	68	
	4:00 P.M.	99.	78	
July 26	8:00 A.M.	97.8	78	
	4:00 P.M.	98.8	78	
July 27	8:00 A.M.	98.	76	
	4:00 P.M.	98.6	78	
July 28	8:00 A.M.	97.4	70	18
July 29	8:00 A.M.	98.2	68	18
	4:00 P.M.	98.	80	20

Urine and Blood Urea

PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE				SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO₃ RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.									gm.	gm.					
8	1350	Acid	1026	Neg.	Pos.	Pos.	Neg.	—	0.56	—	7.56	—	—	—	Neg.	Neg.
9	500	"	1026	Neg.	Pos.	Pos.	Neg.	—	0.64	—	3.20	—	—	—	Neg.	Neg.
10	950	"	1022	Neg.	Pos.	Pos.	Neg.	0.49	0.28	4.65	7.66	—	—	—	Neg.	Neg.
11	600	"	1022	Neg.	Pos.	Pos.	Neg.	—	0.06	—	0.36	Neg.	—	Neg.	Neg.	Neg.
12	900	Slight	1018	Neg.	Pos.	Pos.	Neg.	0.40	0.30	3.60	2.70	Neg.	—	Neg.	Neg.	Neg.
13	970	Acid	1020	Neg.	Pos.	Pos.	Neg.	0.73	—	7.08	—	—	—	—	Neg.	Neg.
14	850	"	1025	Neg.	Pos.	Pos.	Neg.	1.26	—	10.71	—	Neg.	—	Neg.	Neg.	Neg.
15	—	Slight	1025	Neg.	Trace	—	Neg.	1.61	0.34	—	—	—	—	—	Neg.	Neg.
16	675	Acid	1015	Neg.	Pos.	—	Neg.	0.40	0.34	2.70	2.30	—	—	Neg.	Neg.	Neg.
17	1425	"	1013	Neg.	Trace	—	Neg.	—	0.52	—	7.41	—	Neg.	—	Neg.	Neg.
18	700	"	1023		Neg.	Neg.	Neg.	0.44	0.78	3.08	5.46	—	Neg.	—	Neg.	Neg.
19	750	"	1025	—	Neg.	Neg.	—	0.52	0.86	3.90	6.54	—	Neg.	—	Neg.	Neg.
20	1100	"	1010	—	Neg.	—	—	—	0.38	—	4.18	—	Neg.	—	Neg.	Neg.
21	620	"	1024	—	Neg.	—	—	—	0.48	—	2.97	—	—	—	Neg.	Neg.
22	1100	"	1010	—	Neg.	—	—	—	0.62	—	6.82	—	Neg.	—	Neg.	Neg.
23	1625	"	1010	—	Neg.	—	—	—	0.54	—	8.77	—	—	—	Neg.	Neg.
24	1400	"	1012	—	Neg.	—	—	—	0.72	—	10.08	—	—	—	Neg.	Neg.
25	1000	"	1010	—	Neg.	—	—	—	0.76	—	7.60	—	—	—	Neg.	Neg.
26	2100	"	1013	—	Neg.	—	—	0.72	0.60	15.12	12.60	—	—	—	Neg.	Neg.
27	1600	Slight	1015	—	Neg.	—	—	0.67	0.60	10.72	9.60	—	—	—	Neg.	Neg.
28	2000	"	1015	—	Neg.	—	—	0.50	0.50	10.00	10.00	—	—	—	Neg.	Neg.
29	1400	"	1015	—	—	—	—									

BLOOD UREA

Blood unobtainable.

PHENOLSULPHONEPHTHALEIN TEST

July 24 1st hour plus 10 min. 70% excreted.
2nd hour 15% "
Total........85%

Smears from furuncles and hordeolum showed only pus and staphylococci.

COLOR OF URINE

8 Medium lemon yellow, cloudy.

9 Medium lemon yellow, translucent.

URINARY SEDIMENT

Uric acid and amorphous urates. Few casts and cylindroids, granular and hyaline casts, epithelial squamous cells with large golden yellow droplets, markedly refractive. Fatty degeneration.

	COLOR OF URINE	URINARY SEDIMENT
11	Darker.	As above, plus calcium oxalate crystals. Fragments of granular casts.
12		As above. Crystals in excess. Few red blood cells, few leucocytes, few granular casts.
13	Medium dark.	
14	Dark.	
15	Normal.	Sediment much improved.
16	Medium dark.	Few fragments of granular casts. Epithelial cells, leucocytes and amorphous urates.
17	Pale.	As above plus few red blood cells.
18	Normal.	Uric acid, amorphous urates, calcium oxalate. Few red and white blood cells. Few granular epithelial cells.
19	Normal.	Abundant uric acid, as above.
20	Normal.	As above.
21	Slightly pale.	As above.
22	Normal.	As above.
23	Slightly pale.	As above and a few granular casts.
24	Slightly pale.	As above.
25	Normal.	Improved, only a few urates and a few granular epithelial cells were found.
26	Pale.	As next above.
27	Pale.	As next above.
28	Normal.	As next above.
29	Normal.	As next above.

BLOOD

Examination of blood sixteen days after gassing.

Erythrocyte count		4,600,000
White count		21,200
Hemoglobin		78%
Differential white count:		
Polynuclears		
Neutrophile	92. %	
Eosinophile	1.5%	
Basophile	.5%	
Lymphocytes		
Large	2.0%	
Small	2.0%	
Transitionals	1.0%	
Large mononuclears, none found		
Myelocytes	1.0%	

The polymorphonuclears show the Arneth scale to the right, older polynuclears. The platelets are greatly increased in number. Many of the red cells are undersized. No nucleated red cells were found.

CASE VI.—In this case there were severe genital burns which developed a severe secondary pyogenic infection. The general skin involvement was less severe, but well marked.

BLOOD

Examination of blood two weeks after gassing.

Erythrocyte count		4,860,000
White count		16,600
Hemoglobin		78%
Differential white count:		
Polynuclears		
Neutrophile	66 %	
Eosinophile	4.5%	
Lymphocytes		
Large	3.0%	
Small	7.5%	
Transitionals	1.5%	
Large basophilic mononuclears	5.5%	
Myelocytes	12.0%	

The blood platelets are increased. There are no changes in the red cells. No nucleated red cells were found.

URINE AND BLOOD UREA

PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE				SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.	PIGMENTS			
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.									gm.	gm.					
8	460	Acid	1024	Neg.	Pos.	Pos.	Neg.	—	0.16	—	0.82	Neg.	—	Neg.	Neg.	Neg.
9	750	"	1015	Neg.	Pos.	Pos.	Neg.	—	0.30	—	2.25	—	—	—	Neg.	Neg.
10	1150	"	1015	Neg.	Pos.	Pos.	Neg.	0.38	0.14	4.38	1.61	Neg.	—	Neg.	Neg.	Neg.
11	620	"	1024	Neg.	Pos.	Pos.	Neg.	—	0.38	—	7.45	—	—	—	Neg.	Neg.
12	630	"	1024	Neg.	Trace	Trace	Neg.	0.58	1.16	3.65	7.31	—	—	—	Neg.	Neg.
13	300?	"	1018	Neg.	Trace	Trace	Neg.	0.36	—	1.08	—	—	—	—	Neg.	Neg.
14	900	"	1020	Neg.	Pos.	Pos.	Neg.	1.56	—	14.04	—	Neg.	—	Neg.	Neg.	Neg.
15	NO SAMPLE															
16	NO SAMPLE															
17	1600	Acid	1018	Neg.	Pos.	Pos.	Neg.	—	0.40	—	6.40				Neg.	Neg.
18	LEFT THE INFIRMARY															

BLOOD UREA	PHENOLSULPHONEPHTHALEIN TEST
Blood unobtainable.	Patient left before the apparatus was secured.

	COLOR OF URINE	URINARY SEDIMENT
8	Turbid. Deep lemon yellow.	Amorphous urates and uric acid crystals in showers. Few leucocytes. Few hyaline casts.
9	Light lemon, cloudy.	
10	Lighter.	
11	Darker again.	As above plus calcium oxalate crystals in great numbers. Granular as well as hyaline casts. Epithelial cells, both renal and bladder.
12	Normal.	As above except no casts were noted.
13	Normal.	
14	Lighter, normal.	
15	Normal.	
16	Normal.	
17	Normal.	Few uric acid and amorphous urates. Few fragments of granular casts. Few red and white blood cells.
18	Normal.	

CASE VII.—Comparatively mild case of mustard gassing. Slight burns of genitals, axillæ and in the bends of the elbows. General erythema of skin over entire body.

BLOOD

Examination of blood two weeks after gassing.

Erythrocyte count		5,300,000
White count		19,500
Hemoglobin		100%
Differential white count		
Polynuclears		
Neutrophiles	71.5%	
Eosinophiles	5.5%	
Lymphocytes		
Large	3.5%	
Small	10.5%	
Transitionals	.5%	
Large basophilic mononuclears	6.0%	
Myelocytes	2.5%	

There is an increase in the normal granular mononuclears. The blood platelets are increased. No nucleated reds, or other changes in the red cells, were found.

URINE AND BLOOD UREA

	PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE			SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.		PIGMENTS		
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.									gm.	gm.					
8	575	Acid	1026	Neg.	Pos.?	Pos.?	Neg.	—	0.82	—	4.62	—	—	—	Neg.	Neg.
9	1000	"	1027	Neg.	Pos.	Pos.	Neg.	—	0.52	—	5.20	—	—	—	Neg.	Neg.
10	1000	"	1027	Neg.	Pos.?	Pos.?	Neg.	0.38	0.14	3.80	1.40	—	—	—	Neg.	Neg.
11	900	"	1020		Pos.	Pos.	Neg.	—	0.12	—	1.08	Neg.	—	Neg.	Neg.	Neg.
12	1450	"	1019	Neg.	Neg.	Neg.	Neg.	0.54	0.34	7.83	4.93	Neg.	—	Neg.	Neg.	Neg.
13	250?	"	1027	Neg.	Pos.	Pos.		1.12	—	2.80?	—	Neg.	—	Neg.	Neg.	Neg.
14	600	"	1025	Neg.	Pos.	Pos.	Neg.	2.26	—	13.56	—	Neg.	—	Neg.	Neg.	Neg.
15	—	"	1025	Neg.	Neg.	Neg.	Neg.	1.32	0.80	—	—	—	Neg.	—	Neg.	Neg.
16	NO SAMPLE															
17	400?	"	1023		Neg.	—	Neg.	—	0.52	—	2.08?	—	Neg.	—	Neg.	Neg.
18	900	Neut.	1025		Pos.	Pos.	Neg.	0.48	0.54	4.32	4.86	—	Neg.	—	Neg.	Neg.
19	600?	Acid	1025		Neg.	Neg.		0.48	0.86	2.88	4.56	—	Neg.	—	Neg.	Neg.
20	550	"	1025		Neg.	Neg.	—	—	0.30	—	1.65	—	Neg.	—	Neg.	Neg.
21	590	"	1027		Trace	Trace	—	—	0.20	—	1.18	—	Neg.	—	Neg.	Neg.
22	900	"	1017		Trace	Trace	—	—	0.38	—	3.42	—	Neg.	—	Neg.	Neg.
23	565	"	1024		Neg.	Neg.	—	—	0.70	—	4.65	—	Neg.	—	Neg.	Neg.
24	500	"	1025		Neg.	Neg.	—	—	0.72	—	3.60	—	—	—	Neg.	Neg.
25	LEFT THE HOSPITAL															

BLOOD UREA

July 10 .0264 Gm. per 100 c.c. of blood

PHENOLSULPHONEPHTHALEIN

1st hr. plus 10 min.	60%	excreted
2nd hr.	20%	"
Total..........	80%	"

URINARY SEDIMENT

8	Few amorphous urates and uric acid crystals. Few cylindroids and granular casts. Few epithelial cells.
11	Amorphous urates. Few uric acid crystals and calcium oxalate crystals. Few hyaline and granular casts and cylindroids. Leucocytes and a few red blood cells and epithelial cells.
12	Few amorphous urates. Few squamous epithelial cells, otherwise normal.
17	Abundant amorphous urates, few uric acid crystals. Few leucocytes and granular epithelial cells.
18	Sediment crystalline in character. Abundant uric acid and urates, numerous calcium oxalate crystals. Few leucocytes and granular epithelial cells.
19	Few amorphous urates and uric acid and calcium oxalate crystals.
20	Abundant amorphous urates, uric acid and calcium oxalate. Triple phosphates. Few leucocytes. Few granular epithelial cells.
21	Few amorphous urates, uric acid, calcium oxalate; few hyaline and few fragments of blood casts. Few granular epithelial cells.
22	Amorphous urates. Few calcium oxalates and triple phosphates.
23	Excess of amorphous urates and triple phosphates, otherwise negative.

CASE VIII.—Mild case. Recovery.

URINE AND BLOOD UREA

PHYSICAL AND CHEMICAL CHARACTERISTICS OF THE URINE				SUGAR GLUCOSE	ALBUMIN		ACIDOSIS DIACETIC ACID	RENAL FUNCTIONAL EFFICIENCY				DIAZO SUB.	PIGMENTS			
DATE	URINE OUTPUT AMT. IN 24 HRS.	REACTION	SPECIFIC GRAVITY	FEHLING'S SOLUTION	HELLER'S HNO_3 RING TEST	ACETIC AC. FERROCYANIDE	FERRIC CHLORIDE	QUANT. UREA GM. PER 100 C.C.	QUANT. CHLORIDE GM. PER 100 C.C.	UREA OUTPUT IN 24 HRS.	CHLORIDE OUTPUT IN 24 HRS.	SULPHANILIC AC. EHRLICH'S DIAZO	DIMETHYLAMINOBENZALDEHYDE UROBILINOGEN	BROMIN WATER MELANIN	GMELIN'S TEST FOR BILE	FOAM TEST FOR BILE
July	c.c.									gm.	gm.					
8	585?	Acid	1030	Neg.	Pos?	Pos.	Neg.	—	0.22	—	1.28	—	—	—	Neg.	Neg.
9	450?	"	1025	Neg.	Pos.	Pos.	Neg.	—	0.22	—	.99	—	—	—	Neg.	Neg.
10	950	"	1017	Neg.	Pos.	Pos.	Neg.	0.25	0.36	2.37	3.42	—	—	—	Neg.	Neg.
11	500?	"	1023		Pos.	Pos.	Neg.	—	0.40	—	2.00	Neg.	—	Neg.	Neg.	Neg.
12	1125	"	1015	Neg.	Trace	Trace	Neg.	0.43	0.38	4.83	4.27	Neg.	—	Neg.	Neg.	Neg.
13	—	"		Neg.				0.78	—	—	—					
14	920	Alk.	1025	Neg.	Pos.	Pos.	Neg.	0.12	—	1.10	—	Neg.	—	Neg.	Neg.	Neg.
15	NO SAMPLES SUBMITTED AFTER THE ABOVE EXAMINATIONS.															

	BLOOD UREA	.0312 gm. per 100 c.c. NO FURTHER DATA OBTAINABLE.
8	URINARY SEDIMENT	Calcium oxalate crystals. Few granular casts and cylindroids. Epithelial cells. and leucocytes.
11		Amorphous urates. Small granular casts. Many epithelial cells (renal and bladder type). Few red and white blood cells.
12		Excess of amorphous urates, few uric acid, few granular casts. Red blood cells? Granular bladder epithelial cells.

BLOOD

Hemoglobin, 75 per cent. No other examination made.

CASE IX.—Mild case. Recovery.

TEMPERATURE, PULSE AND RESPIRATION

		T.	P.	R.
July 11		Normal		
July 12		Normal		
July 13		Normal		
	4:00 P.M	97.6	76	
July 14		Normal		
July 15		Normal		
July 16		98.4	78	
	4:00 P.M.	98.8	80	
July 17	7:30 A.M.	98.	76	
	4:00 P.M.	98.6	88	
July 18	7:30 A.M.	98.2	78	
	4:00 P.M.	98.2	74	
July 19	8:00 A.M.	98.	78	
	4:00 P.M.	98.4	70	
July 20	7:30 A.M.	98.	76	
	4:00 P.M.	98.6	80	
July 21	7:30 A.M.	97.8	70	
July 22	7:30 A.M.	98.	80	
	4:00 P.M.	98.6	82	
July 23	8:00 A.M.	98.	68	
	4:00 P.M.	98.	80	18

Temperature, Pulse and Respiration

July 24	8:00 A.M.	98.	80	18
	4:00 P.M.		84	20
July 25	8:00 A.M.	98.	76	18
	4:00 P.M.	98.6	82	
July 26	8:00 A.M.	98.	78	
	4:00 P.M.	98.	82	
July 27	8:00 A.M.	98.	80	
	4:00 P.M.	98.6	80	
July 28	8:00 A.M.	97.8	76	
	4:00 P.M.	98.6	76	
July 29	8:00 A.M.			
	4:00 P.M.	98.4	74	

Urine and Blood Urea

Physical and Chemical Characteristics of the Urine				Sugar Glucose	Albumin		Acidosis Diacetic Acid	Renal Functional Efficiency				Diazo Sub.	Pigments			
Date	Urine Output Amt. in 24 Hrs.	Reaction	Specific Gravity	Fehling's Solution	Heller's HNO_3 Ring Test	Acetic Ac. Ferrocyanide	Ferric Chloride	Quant. Urea Gm. per 100 c.c.	Quant. Chloride Gm. per 100 c.c.	Urea Output in 24 Hrs.	Chloride Output in 24 Hrs.	Sulphanilic Ac. Ehrlich's Diazo	Dimethylaminobenzaldehyde Urobilinogen	Bromin Water Melanin	Gmelin's Test for Bile	Foam Test for Bile
July	c.c.									gm.	gm.					
17	550	Acid	1024	Neg.	Neg.	Neg.	Neg.	—	0.58	—	3.19	Neg.	Neg.	Neg.	Neg.	Neg.
18	650	"	1018	Neg.	Neg.	Neg.	Neg.	0.49	0.70	3.18	4.55	—	Neg.	—	Neg.	Neg.
19	1100	"	1015	Neg.	Neg.	Neg.	Neg.	0.32	0.60	3.52	6.60	—	Neg.	—	Neg.	Neg.
21	1050	"	1015	—	Neg.	Neg.	Neg.	—	0.78	—	8.19	—	Neg.	—	Neg.	Neg.
22	500	Neut.	1017	—	Neg.	Neg.	Neg.	—	0.58	—	2.90	—	Neg.	—	Neg.	Neg.
23	820	"	1017	—	Neg.	Neg.	Neg.	—	0.34	—	2.78	—	—	—	—	—
24	1850	Acid	1012	—	Neg.	Neg.	Neg.	—	0.70	—	12.95	—	—	—	—	—
25	1150	"	1013	—	Neg.	Neg.	Neg.	—	0.38	—	4.37	—	—	—	—	—
26	700		1025	—	Neg.	Neg.	Neg.	1.6	0.36	11.20	2.52	—	—	—	—	—
27	1050		1015		Neg.	Neg.		0.72	0.70	7.56	7.35	—	—	—	—	—
28	400?	Acid	1023		Neg.	Neg.		0.84	0.66	3.33	2.64	—	—	—	—	—
29	700	"	1017		Neg.	Neg.		—	—	—	—	—	—	—	—	—

PHENOLSULPHONEPHTHALEIN TEST

1st hr. plus 10 min.	60%	excreted.
2nd hr.	10%	"
Total........	70%	"

URINARY SEDIMENT

17	Few amorphous urates, few leucocytes, few red and white blood cells, few granular epithelial cells.
18	Crystalline in character consisting largely of uric acid and amorphous urates. Otherwise normal.
19	Excess of uric acid and amorphous urates. Otherwise negative.
21	Abundant amorphous urates. Otherwise negative.
22	Crystalline. Large amount amorphous urates. Some triple phosphates, otherwise negative.
23	As on previous day, less in amount.
24	As on previous day, still less in amount.
25	Excess amorphous urates, triple phosphates, otherwise negative.
26	As next above.

Case Group X.—All mild cases with recovery.

Temperature, Pulse and Respiration

		T.	P.	R.
	CASE X-A			
July 27	8:00 A.M.	97.8	68	
	4:00 P.M.	98.4	74	
July 28	8:00 A.M.	97.8	68	
	4:00 P.M.	98.8	76	20
July 29	8:00 A.M.	97.	68	18
	4:00 P.M.	98.2	80	
	CASE X-B			
July 22	7:30 A.M.	97.8	78	
	4:00 P.M.	98.4	80	
July 23	8:00 A.M.	97.6	72	
July 24	8:00 A.M.	97.	76	
	4:00 P.M.	98.6	78	
July 25	8:00 A.M.	97.6	78	
	4:00 P.M.	98.6	78	
July 27	8:00 A.M.	98.4	74	
July 28	8:00 A.M.	97.	68	
July 29	8:00 A.M.	Normal		
	4:00 P.M.	98.	76	
	CASE X-C			
July 23	10:00 P.M.	97.6	70	19
July 24	8:00 A.M.	97.6	74	20
	4:00 P.M.	98.2	76	20
July 25	8:00 A.M.	98.	74	18
	4:00 P.M.	98.	74	
July 26	8:00 A.M.	97.8	74	
	4:00 P.M.	98.	76	
July 27	8:00 A.M.	97.8	74	
	4:00 P.M.	98.4	74	
July 29	8:00 A.M.	97.4	76	18
	4:00 P.M.	98.6	80	20
July 29	8:00 A.M.	97.6	76	
	4:00 P.M.	98.2		
	CASE X-D			
		Normal	Normal	Normal

Urine and Blood Urea

	Physical and chemical characteristics of the urine		Sugar	Albumin							
	Reaction	Specific gravity	Fehling's solution	Heller's HNO_3 ring test	Acetic ac. ferrocyanide	Heat and nitric acid	Heat and acetic acid	Per cent chloride gm. per 100 c.c.	Color	Sediment	
A.*	Acid	1022	Neg.	Neg.	Neg.	Neg.	Neg.	0.38	Clear	Normal.	Negative.
B **	"	1020	Neg.	Neg.	Neg.	Neg.	Neg.	0.54	"	"	Negative.
C.***	"	1020	Neg.	Neg.	Neg.	Neg.	Neg.	0.78	"	"	"
D.****	"	1030	Neg.	Neg.	Neg.	Neg.	Neg.	0.56	"	"	Numerous leucocytes, otherwise negative.

PHENOLSULPHONEPHTHALEIN TEST

A.	10 min. plus 1st hr.	60% excreted.	2nd hr. 15%.	Total 75%.
B.	10 min. plus 1st hr.	50% excreted.	2nd hr. 30%.	Total 80%.
C.	10 min. plus 1st hr.	55% excreted.	2nd hr. 20%.	Total 75%.

NOTE.—These were all comparatively mild cases, and they were used more or less as controls.

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*A. Had had large burns of the feet and smaller ones of the hands. His face was erythematous and his eyes showed acute congestion on the more or less chronic conjunctivitis.

**B. Had had severe hand burns, and a very intense conjunctivitis.

***C. Had had a chronic mild conjunctivitis, and aphonia.

****D. Had no signs of irritation.

BLOOD: These cases showed no blood changes.

General Discussion of the Results

The chemical and microscopic laboratory examinations were carried out as completely as was possible and the negative results were charted as well as the positive pathologic findings. The negative results will serve not only as a guarantee that the specific examinations have been made, but will also furnish a broader basis for further work along this line. Some reactions were found to be negative throughout the series of cases. Fehling's solution failed to reveal any glucose or other reducing substance in these urines. The dilute ferric chloride test never gave the heat labile Burgundy-red reaction of diacetic acid, and on this basis a definite acidosis is ruled out. Of course we can not conclude anything concerning the height of the alkali reserve of the blood from this finding. It may be, and probably is, quite low as we may roughly conclude from the markedly acid urinary reaction and the sediment. Ehrlich's sulphanilic-hydrochloric acid and sodium nitrite reaction for diazo substances was found to be negative in every instance. No melanin reaction was ever noted in the several bromine water oxidizing tests for the pigment. Bile pigments were never found in the urine in quantities sufficient to give the play of colors with fuming nitric acid, and the foam test was always negative.

The daily 24-hour urinary output was at first very low in most cases, and the specific gravity was correspondingly high with the exception of Case I and Case II. In Case I, there was no urine output during the last 24 hours of life, but the anuria was not absolute as there were found 60 c.c. of urine in the bladder at autopsy. However, catheterization nine hours before death had failed to produce a specimen. In Case II, there was intense thirst, and the polydipsia kept the urinary secretion fairly high and the concentration fairly moderate. In all the other cases the forced ingestion of fluids brought the urine output fairly high and reduced the concentration.

The urine in these cases showed uniformly a high acidity. The degree of acidity was in proportion to the severity of the case and was only slightly reduced even with the marked dilution of the urine due to forced ingestion of fluids. The specific gravity varied with the urinary output; it was high at first, but became lower with the dilution of the urine. The amount of albumin present was greatest in the most severe cases and gradually decreased with scientific management and disappeared first in the less severe and eventually even in the more severe cases. In the mildest ones, Case IX and Case Group X, no albuminuria was ever detected.

The urine urea, both the percentages and the quantitative outputs, and the urine chlorides, percentages and quantitative outputs, were low at first in all fairly severe cases, but under the treatment the output of these substances gradually increased in amount, and, in the milder cases, reached a fairly normal level. These figures serve as a fair index of the impaired renal functional efficiency, especially when considered with the blood urea, and an approximate average of the sodium chloride intake.

The only trace of any pathologic pigment in the urine was the reaction of the urine to dimethylaminobenzaldehyde for urobilinogen in the severe cases, Cases II and III only. This might be interpreted as indicating a slight temporary functional impairment of the liver.

The microscopic examination of the centrifugated urine sediment substantiates the diagnosis of renal irritation that was made on the basis of the chemical and physical examination of the urine. The quantity of pathologic constituents in the sediment corresponded exactly with the severity of the cases as indicated by other findings. There were hyaline and granular casts, red and white blood cells, renal and bladder epithelial cells, amorphous urates and uric acid crystals in great numbers. At times calcium oxalate crystals, and only occasionally, the sediment of alkaline fermentation, triple phosphates, ammonium urates and calcium carbonates, were found. The sediments all improved markedly and cleared up under the physiologic therapy that was applied.

The blood ureas ranged from 10 mg. per 100 c.c. of blood in the most severe cases to 26 mg. per 100 c.c. of blood in the least severe cases. These findings together with the diminished urea output may be taken as evidence of a renal insufficiency.

The phenolsulphonephthalein excretion tests could not be made until the renal condition had practically cleared up, so far as could be determined by the chemical and microscopic examinations of the urine. The amounts excreted were high, to the extent of even suggesting a hyperpermeability. In only one case (No. III) was there any indication at all of a slow excretion of substances.

Most of the hematologic work on our cases was done between the tenth and fourteenth days after the gassing. There was noted a slight decrease in the number of erythrocytes; this decrease was most marked in the more severe cases. In Case I, the count ran as low as three and one-half million red blood cells with a hemoglobin of 70 per cent, a fairly severe secondary anemia. Even this most severe case on the tenth day after the gassing, nine hours before death, showed a persistent fairly high leucocytosis and no signs of a terminal leucopenia in spite of a definite loss of resistance against the destructive process and the secondary infection. This case showed an apparent decrease in the number of blood platelets which finding differs from that in all the succeeding cases, though the later smears in Case II toward the end also showed fewer platelets, while the earlier smears showed a marked increase in the number of these constituents.

Case II, as all the other succeeding cases except the last one, showed a more moderate anemia with the erythrocyte count not falling below four million and the hemoglobin totaling about 75 per cent. The leucocyte counts in Case II were seen to fall from a 29,700 leucocytosis at the tenth day to a 10,800 leucocytosis on the twenty-fifth day, the day on which he died. This was taken as an index of the gradual loss of ground or resistance in the fight.

The count remained high enough even at the end, to be considered a mild leucocytosis. The blood platelets were markedly increased at first, but were not so at the end.

Case III, aside from the slight secondary anemia, showed a very gradual drop from a leucocytosis of 25,000 to one of 15,000. This drop, however, was accompanied by a gradual general improvement and a clearing up of the sloughing and secondary infection. There was also a definite increase in the number of blood platelets.

Case IV showed the slight secondary anemia and a marked leucocytosis of 25,000 two weeks after having been gassed.

Case V showed also the slight secondary anemia and a leucocytosis of 21,200. The blood platelets were also noted to be increased in numbers.

Case VI showed also a mild secondary anemia and a moderate leucocytosis. The blood platelets were also noticeably increased.

Case VII, the least severe of the series of generally gassed cases, showed no secondary anemia. A fairly high leucocytosis, about 20,000, was found, in spite of the absence of any marked suppuration or generalized secondary infection.

Summarizing the study of the blood in these seven cases of severe mustard gas burns we see that it shows a secondary anemia (reduction of both the number of red blood cells and the hemoglobin), a polymorphonuclear leucocytosis with disturbances in the differential count, such as an increase in the number of bone marrow elements (myelocytes, myeloblasts, bone marrow mononuclears and lymphocytes) and a definite eosinophilia. An excess of young forms of white cells is found. There is also an apparent increase in the number of blood platelets. No evidences of hemolysis were found. A very few red blood cells showing polychromasia and stippling were seen. There was no leucopenia observed in any of these cases, either during the course, or, in the two fatal cases, as an agonal phenomenon. The differential count indicates a disturbance of the bone marrow in the white cell forming group rather than in the red cell forming group. These changes can perhaps be explained by the coincident infection of the skin lesions and the respiratory tract, which all of these cases showed to a greater or less degree. The blood changes ran a fairly parallel course to the severity of the infection. The eosinophilia can be referred to the skin condition, perhaps also to the bronchial.

Under the miscellaneous laboratory examinations we must include the findings in the sputum. In general we may say that the sputum was never blood-tinged but was always more or less mucopurulent in character depending on the severity of the pulmonary affection. In Case III with a bronchopneumonia the sputum was most purulent, frothy and markedly foul in odor, and abundant in amount. On one occasion the patient expectorated a pinkish fibrin-like cast of a bronchus. Smears of this material were found to contain a mixed culture of streptococci and one of the long thick bacillary types of organisms that are found in the mouth. It seemed rational to consider these organisms as the probable etiologic factors in the secondary bronchopneumonia in this case.

The examination of the feces morphologically was negative in most cases, but in Case II at increasing intervals during the last two weeks of his life the patient passed bright red and some slightly changed blood in his involuntary stools. In his last few days the amount of blood passed gradually increased as the patient grew weaker.

Smears of the young furuncles and pus from the old furuncles always showed a few groups of staphylococci, many degenerating polynuclear leucocytes and much debris.

The temperature charts showed febrile reactions with corresponding pulse and respiration rise, only during the presence and persistence of secondary infection. The high pulse rate in the severer cases would lead one to suspect myocardial injury. This suspicion, however, is not substantiated by the pathologic examination of the heart muscle at autopsy.

Comparing our results with the few reports of research along similar lines found in the literature, the only one of any importance on blood changes due to gassing is that of Miller (*Journal of the Royal Army Medical Corps*, January, 1918, xxx, p. 76). After an extensive amount of work he reported a new blood change in gas poisoning as follows:

1. In cases of gas poisoning in which symptoms persist, there is an increase in the number of lymphocytes relative and absolute in the circulating blood. In slight cases this may not be beyond the normal limits or in excess of what may be met with from other causes. In any marked case, however, the changes are sufficiently striking to be of some importance in cases where the medical officer is in doubt as to the reliance to be placed upon the statements of men complaining of having been gassed.

2. The blood change is elicited by a differential count of the leucocytes, and it may be taken that a count in which the percentage of lymphocytes approaches that of the polymorphonuclear leucocytes indicates that the patient is still suffering from the effects of the gassing, i. e., provided there is no other complicating disease present which might produce a similar change. A slight relative lymphocytosis is not an uncommon finding in men from overseas, or in anyone, so that no great reliance can be placed upon the signs unless the percentage of lymphocytes approaches closely that of the polymorphonuclear cells.

3. The cell which is increased is the ordinary small lymphocyte of the blood. There may be in some cases a diminution in the number of polymorphonuclear leucocytes which will of course accentuate the sign, but the increase of lymphocytes is an absolute one. Moreover, it appears in cases with a high leucocyte count.

4. The change is one which develops early, probably within a month of the gassing and continues for a long time; in cases with persistent symptoms, for at least eighteen months.

5. The change appears to be independent of the kind of gas and it is shown by patients exhibiting many varieties of symptoms.

Our findings are not in accord with the above conclusions for all gases, and our cases may not be comparable with his. It seems to us to be questionable whether Miller studied and included the blood findings in cases of mustard gas poisoning. He mentions only the two groups of drift gases and shell gases, and does not differentiate the subclasses chemically at all. His last article published early this year came late enough to have the blood changes produced by mustard gas included, yet no mention is made of it and on the basis of the symptoms described we can not conclude that dichlorethylsulphide cases were studied in this series. We discuss this paper because Miller claims that his sign is present in all chronic gassed cases regardless of the kind of gas to which they had been exposed and independent of the symptomatology presented. Then, too, the pathologic conditions which he favors as the most probable etiologic factor in the production of the lymphocytosis, that is, the chronic inflammatory change in the respiratory tract and in the gastric mucosa, could very well be present in chronic mustard gas cases. We do not think that such conclusions can be drawn for all types of gassing as yet, but the decision must rest with the results obtained from further studies of cases in which the chemical nature of the gas is known.

Moreover, our findings do not agree at all with those of Pissarello; but it is possible that his negative findings in the urine were due to the mild character of his cases, corresponding to those in our Case Group X.

Mandel and Gibson's observation on the frequency of albuminuria in cases of mustard gas poisoning is confirmed by our work.

Conclusions

1. Mild cases of mustard gas burns of the skin show no changes in the blood or urine.

2. Moderately severe and severe cases of mustard gas burns of the skin with some involvement of the upper respiratory tract show after the first week definite changes in urine, blood urea and blood.

3. The urinary changes consist in a diminution of the urinary output, increased concentration and acidity, albuminuria, and diminished urea and chloride output. In the sediment there may be found casts, renal epithelium, red blood cells and an increased number of leucocytes. Under forced fluids prompt improvement occurs.

4. Coincident with these urinary changes the blood urea is found to be high, but approaches normal with the improvement in the urinary condition when fluids are forced.

5. The blood shows a slight secondary anemia with a well-marked polymorphonuclear leucocytosis, a definite eosinophilia, and the appearance of myelocytes and young forms of leucocytes. The blood platelets were usually increased. No evidence of hemolysis was found. These changes indicate a disturbance in the white cell formation rather than in the red blood cell group. No leucopenia was noted at any time. The leucocytosis reached its height coincidently with the height of the secondary infection and fell with the improvement of the infection.

6. The temperature, pulse and respiration charts show in the severe cases an initial period of shock. With the development of the necrosis and the secondary infection there is a corresponding febrile reaction.

7. The bacteriologic examination of the infected skin lesions and furuncles showed constantly the presence of staphylococcus pyogenes aureus. In the one bronchial cast obtained streptococci were present.

8. We believe that the changes in the blood and urine may be interpreted as dependent upon the secondary infection and, in part, possibly, to the absorption of toxic products from the necrotic skin, rather than to any direct toxic action of mustard gas.

My thanks are due to Doctor A. S. Warthin for directing this work, to Captain L. L. Roos for the privilege of studying the cases under his care and to Doctor C. V. Weller for many helpful suggestions.

BIBLIOGRAPHY

[1]Mandel and Gibson: The Clinical Manifestations and Treatment of Gas Poisoning, Jour. Am. Med. Assn., December, 1917, lxix, No. 23, p. 1970.

[2]Pissabello, Carlo: Relazione sugli effeti morbosi delle granate cariche ad "Yprite." Giornale di Medicina Militare, 1918, lxvii, 128.

[3]Miller and Rainy: A Note on the Blood Changes in Gas Poisoning, Lancet, London, 1917, i, 19.

Miller, James: Blood Changes in Gas Poisoning, Lancet, London, 1917, i, 793.

Miller, James: Jour. Roy. Army Med. Corps, January, 1913, xxx, No. 1, p. 76.

[4]Simon, C. E.: Clinical Diagnosis, 1918.

[5]Wood, F. C.: Clinical and Microscopical Diagnosis, 1917.

[6]Todd, J. C.: Clinical Diagnosis, 1918.

[7]Gilbert, Q. O.: Laboratory Methods of Diagnosis, 1918.

Note: Since the above chapter was written there has appeared an article by *E. B. Krumbhaar*, "Rôle of the Blood and the Bone Marrow in Certain Forms of Gas Poisoning" (*Journal of the A. M. A.*, 1919, lxxii, No. 1) dealing with the hematologic examinations made on a series of patients gassed with mustard gas. Krumbhaar concludes that in mustard gas poisoning there is an initial leucocytosis followed by a more or less extreme degree of leucopenia, which persists even in the presence of bronchopneumonia, and is very probably an important contributing factor to the high mortality of severe cases. Should the leucocyte count fall below 1,000 per c.mm. a "myelocyte crisis" may bring about a partial amelioration: but in the two cases observed of this kind, this did not serve to protect them from a fatal outcome. Lessened blood formation is also indicated by the production of anemia without blast cell formation and diminution in the number of blood-platelets. In the earlier stages the coagulation time is decreased, and in the later stages of severe cases it is increased.

Our experience with human cases of mustard gas poisoning, even the fatal cases, and with experimental animal gassing gave results in contradiction to those obtained by Krumbhaar. We have never observed a leucopenia; on the contrary, there is a definite leucocytosis in all severe and moderately severe cases, with a mild secondary anemia, and an increase in the blood-platelets instead of a decrease. There is also very frequently an increase in the eosinophiles.

Pappenheimer (*Society for Experimental Biology and Medicine*, 1919, xvi, p. 92), after intravenous injections in rabbits of impure dichlorethylsulphide obtained from German gas shell, noted in animals surviving to the second day, a marked leucopenia and changes in the bone marrow comparable to those produced by benzol. He suggests that these blood changes may be due to the chlorobenzene or nitrobenzene contained in the shell. A. S. W.

Appendix: Since the papers by Krumbhaar and Pappenheimer have opened up the question of the blood changes produced by dichlorethylsulphide poisoning, we have again taken up this problem and have carried out a series of investigations on animals with the view of settling this question. In rabbits, gassed in the gassing chamber at varying concentrations, there occurs within twenty-four hours following the gassing a distinct concentration of the blood as shown by a polycythemia varying from one to two millions increase, and an increase in the leucocytes. This concentration may last for several days after which the number of red blood cells slowly comes down to normal. With the advent of secondary infection which may take place at any time from the second to seventh day after gassing, there is a leucocytosis which may reach 50,000. Should the animal live and show increasing cachexia as the result of infection, the blood picture of a secondary anemia develops. This, however, has no direct relationship to the toxic action of dichlorethylsulphide. We are, therefore, confirmed in our previous observations that cutaneous, ocular or respiratory gassing with dichlorethylsulphide has no direct action upon the blood or bone marrow.

We give here four selected protocols illustrating these points.

RABBIT 90.—Gassed six hours at a concentration of 1 to 20,000.

	RED COUNT	WHITE COUNT
June 20	4,710,000	7,400
“ 21	5,470,000	16,000
“ 22	5,290,000	9,200
“ 23	5,130,000	17,400
“ 24	5,000,000	18,400
“ 25	5,130,000	13,200
Gassed from 2:45 P.M. to 8:45 P.M., June 27.		
June 28 8:00 A.M.	6,560,000	15,700
2:00 P.M.	7,800,000	13,600
“ 29	5,510,000	49,600
“ 30	4,970,000	14,400
July 1	6,460,000	31,600
“ 2	5,270,000	15,800
“ 3	4,180,000	18,000

Differential Counts

	BEFORE GASSING		AFTER GASSING	
	June 21	June 25	June 28	July 3
Lymphocytes	36%	28%	27 %	15%
Large mononuclears	7%	3%	1.5%	1%
Polynuclears	52%	66%	70 %	81%
Eosinophiles	4%	2%	.5%	3%
Mast cells	1%	1%	1 %	

RABBIT 91.—Gassed six hours at a concentration of 1 to 20,000.

	RED COUNT	WHITE COUNT
June 20	5,860,000	14,000
“ 21	5,720,000	14,000
“ 22	6,000,000	12,800
“ 23	5,560,000	11,400
“ 24	5,070,000	17,600
“ 25	5,890,000	10,800
Gassed from 2:45 P.M. to 8:45 P.M., June 27.		
June 28 8:00 A.M.	7,400,000	34,800
2:00 P.M.	7,080,000	16,000
Died night of June 28-29.		

Differential Counts

	BEFORE GASSING	AFTER GASSING
	June 20	June 28
Lymphocytes	25%	14%
Large mononuclears	3%	2%
Polynuclears	69%	82%
Eosinophiles	3%	2%
Mast cells		

RABBIT 92.—Gassed one hour at a concentration of 1 to 30,000.

	RED COUNT	WHITE COUNT
June 20	5,200,000	10,200
“ 21	4,900,000	17,600
“ 22	4,720,000	13,600
“ 23	4,900,000	14,400
“ 24	5,120,000	15,200
“ 25	5,650,000	10,800
Gassed from 10:00 A.M. to 11:00 A.M. on June 28.		
June 29	6,800,000	12,000
“ 30	5,290,000	14,200
July 1	5,100,000	22,200
“ 2	5,020,000	15,700
Died during night of July 1-2.		

Differential Counts

	BEFORE GASSING	AFTER GASSING	
	June 25	June 29	July 2
Lymphocytes	39%	16%	16%
Large mononuclears	2%	9%	
Polynuclears	53%	73%	84%
Eosinophiles	6%	2%	
Mast cells			

Rabbit 93.—Gassed one hour at 1 to 30,000.

	RED COUNT	WHITE COUNT
June 20	6,100,000	10,000
" 21	6,200,000	9,400
" 22	5,730,000	9,200
" 23	5,590,000	8,600
" 24	5,840,000	10,000
" 25	5,700,000	8,200
Gassed from 10:00 A.M. to 11:00 A.M. June 28.		
June 29	6,250,000	28,000
" 30	6,360,000	11,500
July 1	5,100,000	12,200
" 2	5,640,000	10,500
" 3	6,050,000	9,200

Differential Counts

	BEFORE GASSING	AFTER GASSING
	June 25	July 3
Lymphocytes	32%	28%
Large mononuclears	2%	2%
Polynuclears	60%	70%
Eosinophiles	4%	
Mast cells	2%	

As to the effects of intravenous injections on the blood, it is to be expected that with the rapidly developing cachexia and emaciation due to the intense diarrhea and accompanying complete anorexia in the animals surviving, both the red blood cell and white blood cell counts after an initial rise will fall, the leucocyte count first and more markedly. This in itself may serve as an explanation in part of Pappenheimer's findings, although his suggestion that the German gas used by him for intravenous injections may have contained benzol derivatives in amount sufficient to cause blood changes must also be regarded as a likely possibility.

We have, however, just concluded a series of experiments that show conclusively that intravenous injections of small doses (.01-.006 c.c.) of *pure* dichlorethylsulphide do produce an initial leucocytosis, followed by an extreme leucopenia (250-375) before death, with marked depletion of the bone marrow. Pappenheimer's observations are thereby confirmed. (See page 203.)

CHAPTER VII

THE TREATMENT OF DICHLORETHYLSULPHIDE ("MUSTARD GAS") INJURIES

Very little has been published, or made available to the medical profession, of the treatment of mustard gas injuries. This can be explained, in part at least, by military exigencies, but also, without doubt, chiefly by the fact that the treatment has been largely empirical or experimental.

Mandel and *Gibson* (*Journal American Medical Association,* December 8, 1917) give a summary of the treatment used abroad at the time of their writing. This treatment consists essentially of the use of a 10 per cent sodium bicarbonate solution for the cutaneous burns, irrigation of the eyes with boric acid solution, use of alkalies internally, bleeding for the pulmonary edema, opiates for the paroxysmal cough and treatment of complications as they arise.

Teulières (*Journal de Médecine de Bordeaux,* 1917, xlvi, p. 247; 1918, xlvii, p. 37) writing of the ocular lesions produced by mustard gas says that the treatment consists of the application of warm vapor, the instillation of a collyrium of atropine and iodoform ointment. From his article it would appear that bicarbonate water is used as an eye wash as a first-aid measure to those exposed to the gas.

Teulières and *Valois* (*Archives d' Ophtalmologie,* 1916-17, xxxv, p. 403) again treat of the ocular lesions and state that the treatment that has given the best results is the eye-bath with warm vapor lasting for ten minutes and repeated from four to five times daily. They also give instillations of adrenalin and cocaine solution for the pain and frequent instillations of atropine when the iris is involved.

Giraud (*Journal de Médecine et de Chirurgie,* November 25, 1917, lxxxviii, p. 890) gives the methods used in the French army at that time, as follows: Use of bicarbonate solution at the first-aid station, both for the eyes and the skin burns, followed in the case of the latter by a dressing of Vincent's powder (boric acid and calcium hypochlorite). The lesions of the respiratory tract are given a purely symptomatic treatment of revulsions, opiates and expectorants. He mentions the fact that many men claim to have escaped the toxic action of the gas while smoking.

Pissarello (*Giornale de Medicina Militare,* 1918, lxvii, p. 128) gives the ophthalmologic aspects of mustard gassing, and sums up the treatment as follows: Patient immediately undressed; clothing aired and sunned. Bandage removed from eyes at once, if present, as it may be a cause of corneal abrasion. Bandage a danger in cases of bulbar chemosis. Use light gauze curtain before eyes. Two per cent bicarbonate or boiled sterile water as an eye wash, with warm vapor fomentations, twenty minutes each, three times daily. Avoid bandages and cocaine. Zinc oxide ointment for the lid lesions. For the skin lesions use pomade of vaseline and 10 per cent bicarbonate of soda. Patients should be kept in a warm moist ward to prevent bronchial complications. Keep ward air moist by a boiler of 2 per cent bicarbonate solution. Use this solution as a gargle also. Dover's powder, chloral and bromide mixture, opium and belladonna may be used for cough and nervous symptoms. Pissarello observed no internal toxic action of the gas.

Bandaline and *Poliakoff* (*Bull. de l'Acad. de Médecine*, July 9, 1918, lxxx. p. 30) advise the use of hot-air douches (150° to 180° C.), under pressure of 300 gm., to give relief to the intense pain and insomnia following mustard gas burns. They also advise the use of a "linoserum" (infusion of flaxseed, 1.5 p. 100, 1000 grm.; sodium chloride pure, 9 grms.; filtered and sterilized in autoclave, 20 minutes at 120° C.) to prevent dressings adhering to wound surfaces.

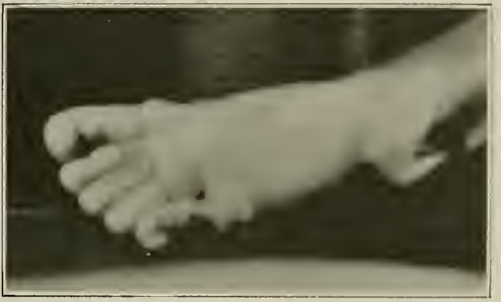

Fig. 144.—Foot 24 hours after exposure of 4 hours in shoe contaminated with mustard gas. Marked tense vesicles. Four hours after exposure, treatment by immersion in Dakin's solution was begun with immediate good results.

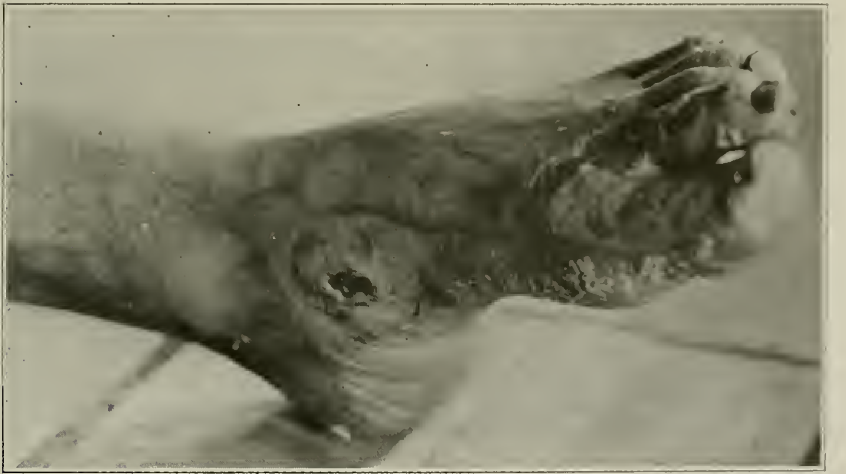

Fig. 145.—Photograph of foot six weeks after contamination of shoe with few drops of mustard gas. Six weeks' treatment with zinc stearate, American oil, and vaseline produced the picture seen in the figure. Within one week after treatment with Dakin's solution and saline baths the lesions were entirely epithelialized, with resulting prompt and complete recovery.

Amantea, G. (*Policlinico, Rome*, 1918, xxv, 893) reports that a 3-5 per cent solution of silver nitrate modifies the action of mustard gas even to the point of annulling its toxic action. Even when the mustard gas has been for some time in contact with the skin the application of silver nitrate solutions is of benefit. For the eye lesions he advises instillations of a one per cent solution or a .25 per cent solution for rinsing the eye and small wounds. For large wounds a 1:1000 solution can be used with proper caution.

Viale, G. (*Policlinico, Rome,* 1918, xxv, 1061) was unable to confirm Amantea's statements in regard to the effective neutralization of mustard gas by silver nitrate. It does not seem to lessen the degree of injury from mustard gas, but after the lesion had reached its full development, the use of silver nitrate seemed to promote the healing process.

Rousseau and *Devaux* (*Journal d. Médecine de Bordeaux,* 1919, xc, p. 149) advise the use of copious applications of hydrogen dioxide to relieve the pain and irritation in mustard gas burns.

The clinical resemblance of mustard gas lesions of the skin to thermal burns has led naturally to the use of alkalies externally and to the application of air-excluding protectives, such as oils, pastes, ointments, pomades, paraffin, oiled paper, dusting powders, etc. The extensive use abroad of a 10 per cent bicarbonate solution is the result no doubt of its employment in the treatment of other forms of gassing.

Protective and Preventive Measures

For the protection of the soldier there have been developed efficient gas masks and gloves and garments composed of fabrics rendered more or less impervious to mustard gas liquid or vapor. It is not permissible at this time to make public the details of such means of protection.

Many substances have also been recommended, such as oils, various fats, ointments, pomades, varnishes, soaps (both plain and filled), water pastes, dusting powders, etc., designed either for the protection of the skin or for the amelioration of the lesion should contact occur. It was early recognized that water and sweat increased the intensity of the action of mustard gas, the most severe lesions occurring when the individuals were warm and perspiring; and the parts of the skin most severely affected were those most likely to be bathed with perspiration or to come in contact with damp clothing, such as the axillæ, flexor surfaces of elbows, genitalia, thighs, etc. Nevertheless, if liquid mustard gas comes in contact with the skin, immediate washing with water will lessen the intensity of the lesion although it may make it more diffuse. Still more effective is washing with tincture of green soap or kerosene. In the case of the standard droplet tests the use of tincture of green soap will effectually prevent any lesion beyond that of an erythema if used within several minutes. Kerosene has a similar protective action. If after the application of the standard droplet, the area is rubbed for fifteen minutes either with tincture of green soap or with kerosene, the lesion rarely progresses beyond an erythema, even after a lapse of ten minutes between the application and the preventive treatment. Inasmuch as mustard gas penetrates into the hair follicles and sweat glands, this prolonged rubbing probably acts in bringing to the surface any mustard gas that may have entered these structures. The kerosene rub was adopted as a routine measure of protection in certain industrial plants. Still more effective, in our opinion, is the use of a chlorinating solution such as Dakin's solution or other preparations yielding hypochlorous acid or available chlorine for the destruction of the mustard gas. In our experience, the use of oils, oint-

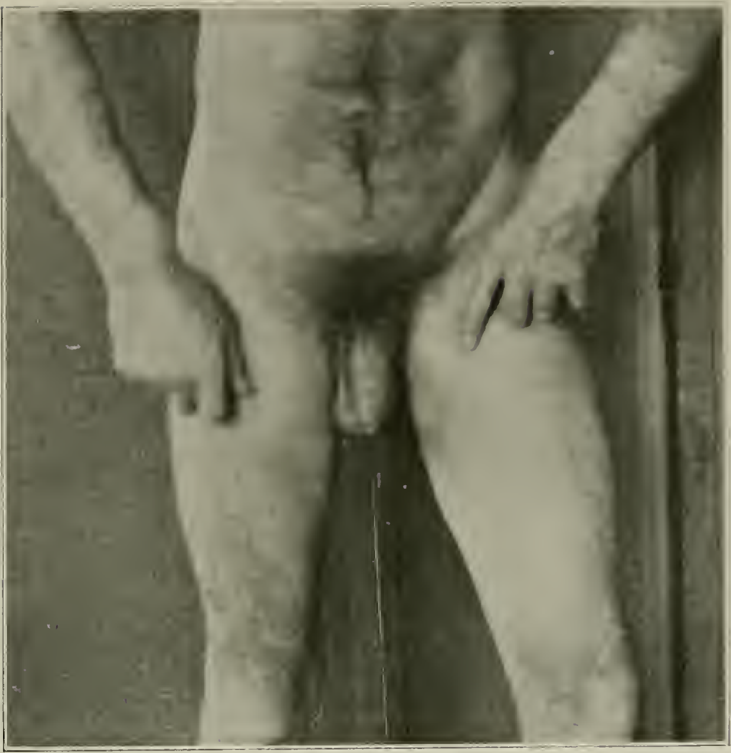

Fig. 146.—One week after 10 to 12 minutes' exposure to strong concentration of mustard gas vapor; erythema and pigmentation of skin; acute urethritis and phimosis. The genital conditions might easily be mistaken for venereal infection.

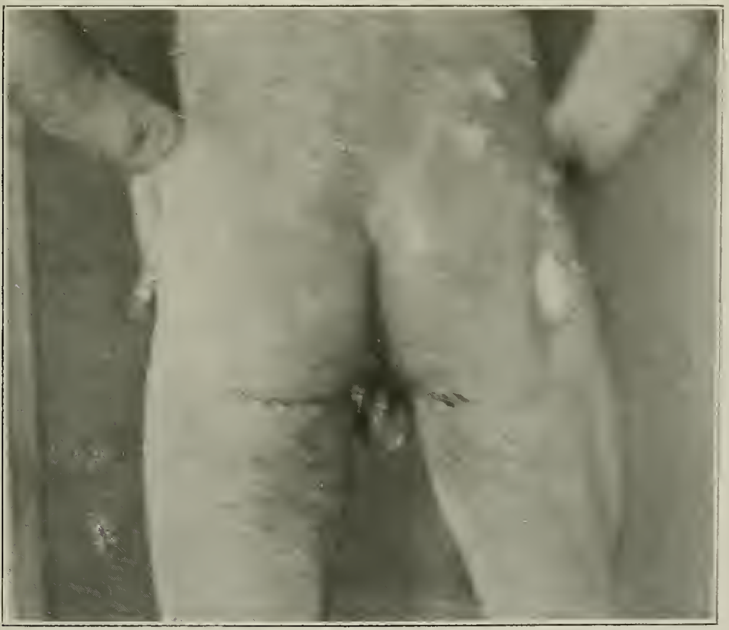

Fig. 147.—Buttocks of same patient as the preceding, taken at the same time, showing desquamation of necrotic epidermis. As in most of the mild cases, the greater severity of the lesions about the genitals and buttocks is well shown.

ments and pastes may actually increase the intensity of the lesion owing to the solution of the mustard gas vapor in these substances. We advise against the use of any paste or ointment unless it is a chlorinating one. During our experimental work, we found that bleaching-powder paste gave complete protection from mustard gas lesions on the hands when applied immediately after any accidental contact with liquid mustard gas. Our experience with lead acetate, silver nitrate, sodium sulphide, magnesium sulphate and potassium permanganate led us to believe that these substances are of little value in lessening the intensity of the lesion and that they may actually increase its severity.

Method of Treatment

From the laboratory standpoint and theoretically it became very evident to us that any form of treatment covering the surface of the injured skin areas and forming an air-excluding and germ-including coating was the worst possible method of treatment. Our animal experiments with zinc stearate and other forms of oily coatings confirmed this view. Inasmuch as mustard gas causes a necrosis, more or less deep, of the skin, cornea and conjunctiva, and mucous membrane of the respiratory tract, the therapeutic problems are as follows:

1. To sterilize the dead tissue and prevent infection of the eschar.
2. To prevent further necrosis by removing pressure.
3. To promote removal of the eschar and rapid regeneration and healing without secondary infections.

Naturally, the use of Dakin's solution suggested itself as an ideal method, particularly because the use of a chlorinating solution would also serve to destroy any mustard gas remaining in the skin, hair follicles, or sweat glands. The use of the bath method, as carried out in the treatment of severe thermal burns and necrotic and suppurative conditions of the skin, seemed an ideal method of treating severe mustard gas lesions, because of the danger of bedsores and secondary necrosis from pressure.

An opportunity of applying these principles to the treatment of mustard gas lesions in human beings presented itself. A number of cases with mustard gas injuries varying from the mildest form up to the most severe and fatal degree were seen by us. When first seen they had been treated for a week by the air-excluding method of zinc stearate, olive oil, mineral oil, oiled paper, etc. The severe cases were all infected, stinking with the odor of gangrene; the injured areas of the skin were gangrenous and dripping with a purulent sanguineous fluid, and large areas of pressure decubitus were developing. An opportunity was afforded for the practical working of our suggestions; and the results justified this method of treatment, although, under the crude and inefficient conditions obtaining, the complete immersion method was not given a full trial. For local lesions, as of the genitals, the hip bath proved the efficacy of this method (see Fig. 151).

We, therefore, believe that the method of treatment outlined below is of great practical value. It is founded upon the pathology of the lesions produced by mustard gas, and is based upon scientific principles. It is not empirical or symptomatic. In practice it has produced good results.

Our Method of Treatment

A. Mild Injuries.—Wash immediately, or better, immerse parts one-half to two hours in Dakin's solution (strength of about 0.5 per cent hypochlorous acid). If too irritating, and when the skin is unbroken this is not likely to be

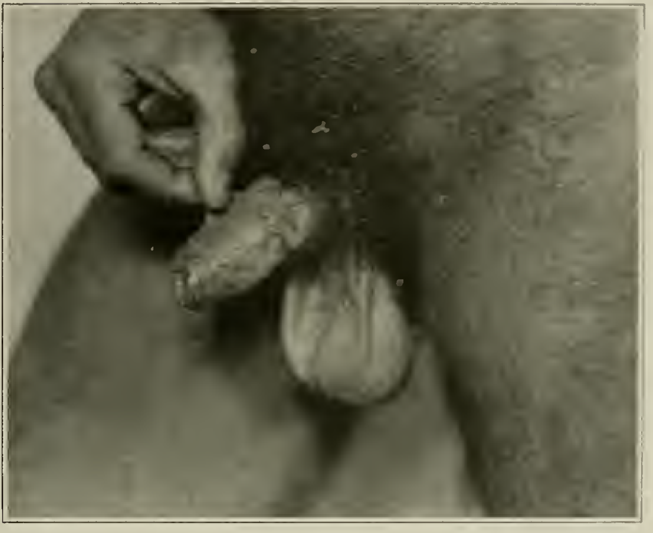

Fig. 148.—Genitals of same patient as the preceding, two weeks after exposure; during these two weeks he had been treated with applications of zinc stearate, vaseline and olive oil, with increasing necrosis of the epidermis. When finally persuaded to use the hip bath of Dakin's solution alternating with saline baths the effects were so prompt and so beneficial to the patient that he became one of the most enthusiastic advocates of the method. The change in the method of treatment effected prompt healing.

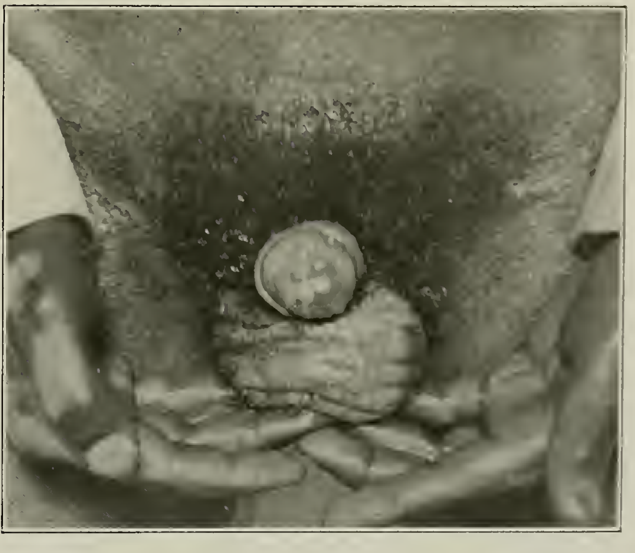

Fig. 149.—Photograph taken two weeks after one-half hour's exposure to strong concentration of mustard gas vapor. During this time patient was treated with zinc stearate and oily-base methods with resultant secondary infection, ulceration and gangrene of the skin of the parts. This patient had tried so many ointments and applications that he was with difficulty persuaded to try the Dakin's and saline hip bath method. On beginning this method of treatment the beneficial effects were so marked that he also became an enthusiastic advocate of the method. Progress of healing from the time of change of treatment uninterrupted.

the case, dilute the solution or shorten time of immersion. If injured surfaces are very large use full bath; for lesions of the genital region use sitz bath. When immersion of parts is not expedient use wet Dakin's dressings or irrigate with Dakin's solution. If the wet treatment (which we consider by far the best) can not be carried out, the application of dichloramine-T in chlorcosane or chloramine-T in sodium stearate may be used. These procedures will serve

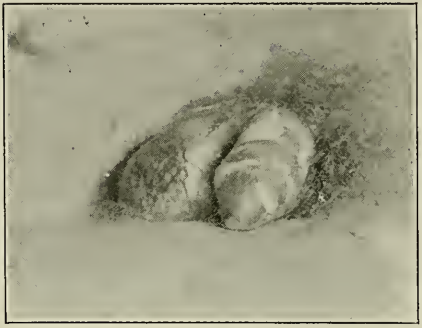

Fig. 150.—Genitals twelve days after three-quarters of an hour exposure to strong concentration of mustard gas. During this time treatment with zinc stearate, etc. Stinking gangrene of the skin of the scrotum and penis. These parts were covered with a tough greenish yellow necrotic membrane, forming a complete cast of the parts and holding the infection and pus beneath it. This membrane had to be removed to permit access of the Dakin's and saline solutions. The condition shown is a very striking example of the bad effects of the grease method of treatment. Such localized genital lesions might very easily be mistaken for venereal sores, as did actually happen in France.

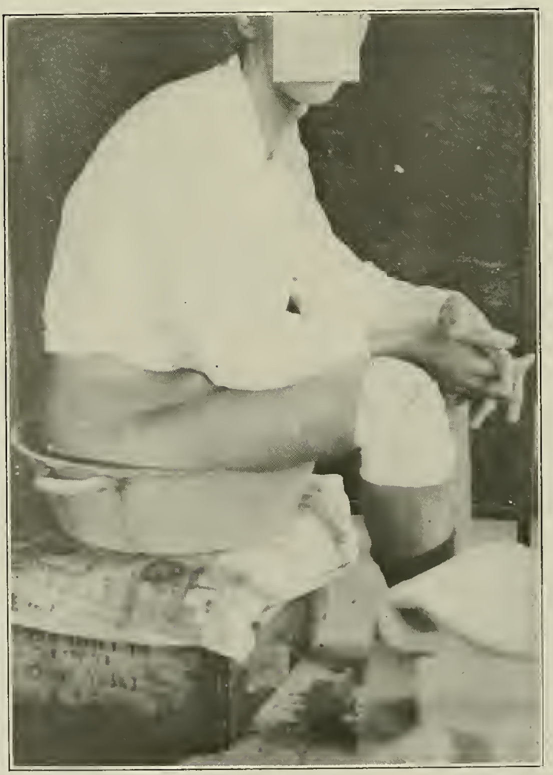

Fig. 151.—Method of applying Dakin's and saline solutions to mustard gas lesions of the genitals. Genitals of this patient shown in Fig. 149.

a double purpose of chlorinating and rendering inactive any dichlorethylsulphide remaining in the skin, hair follicles, etc., and also disinfecting the damaged skin surface. This primary disinfection of the skin is of very great importance in the prevention of the secondary infections that are so often of a serious character. After the Dakin's solution, use wet dressings, irrigation or bath of sterile hypertonic saline (5 to 10 per cent), alternating with the above Dakin's solution and a sterile physiologic saline, according to judgment, about as follows: Dakin's 1 to 2 hours, hypertonic saline 2 hours, physiologic saline 1 hour, and then repeat until lesions appear and extent of injury can be determined. As long as the lesion remains an erythema continue this treatment during the daytime. At night, dry the skin under aseptic precautions, and apply a vanishing surgical cream containing hypochlorous acid or liberating chlorine, of the type of the chlorazene (chloramine-T, 1 per cent, in sodium stearate) surgical cream, or instead, use wet hypertonic saline dressings. Dusting powders are inadvisable because of crusting and possibility of infection. Chloramine-T and dichloramine-T in full strength powder form are too irritating. We have had no experience with Vincent's powder but on general principles would not favor its use. We also advise against the use of silver nitrate, iodine, potassium permanganate, or other local applications. Saturated magnesium sulphate solution proved irritating and no benefits were observed from its use.

In the case of vesicle formation, empty vesicles early under aseptic precautions, by means of a hypodermic syringe or sterile needle with slight pressure upon the vesicle, and allow intact vesicle wall to collapse and seal down upon its base. After this procedure continue with alternating Dakin's and sterile salines, as above. If vesicles are not drained early, the fluid content may, within 4 to 5 hours, coagulate to such an extent that a large coagulum is formed that can not be removed and becomes a possible medium for bacterial growth. It is very important that skin damaged by mustard gas be protected from trauma. Slight injuries, even ordinary pressures of the body, will cause the development of secondary vesicles or decubitus in the injured areas. This phenomenon is analogous to Nikolsky's sign in pemphigoid conditions; and the use of the full bath serves the same purpose as in the treatment of pemphigus and allied diseases.

The use of unguents and ointments with oily bases, such as zinc stearate, olive oil, oleum petrolatum, or any form of crude vaseline or other protecting oil, or such air-excluding and infection-including protectives as oiled paper, paraffin sprays and coatings, such as are employed in the treatment of thermal burns, is strongly condemned by us in the treatment of dichlorethylsulphide injuries. The principle of excluding the air for the purpose of lessening pain in the treatment of thermal burns is not applicable here because of the relative anesthesia of the dichlorethylsulphide lesions in their earlier stages. Exceptions to the above rule are the sodium stearate impregnated with chloramine-T and the chlorcosane solution of dichloramine-T, as in these cases there is an active and persistent germicidal agent present. In the case of denuded surfaces with much pain and when bedsores have developed, the colloidal saline bath is strongly advocated by us. This bath is made as follows: Dissolve one pound of commercial cornstarch and one pound of sodium bicarbonate in 20 to 30 gallons of sterile physiologic salt solution, at a temperature of 90° to 95°.

The patient can be left immersed in this, when necessary, from 15 minutes to 48 hours. The patient should be constantly watched by the nurse. Should pulse become weak, give strychnine or any active digitalis preparation, or remove from bath, and apply blankets and heat.

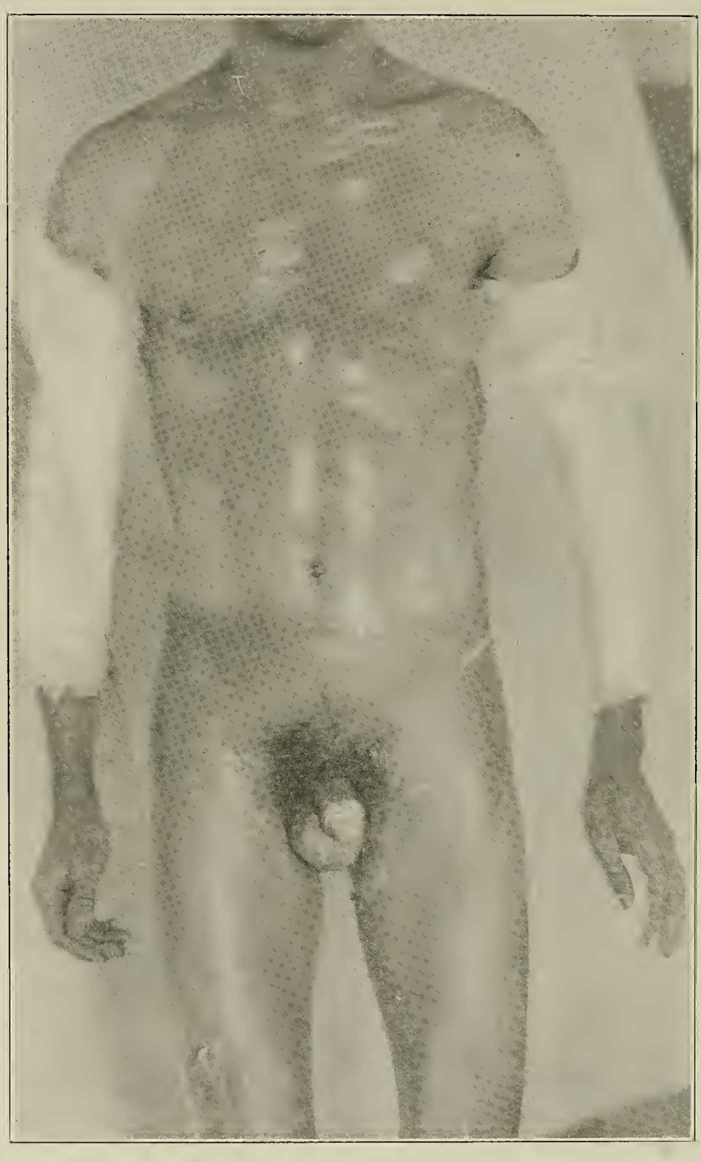

Fig. 152.—Photograph taken one week after 40 minutes' exposure to strong concentration of mustard gas vapor. Treated with grease method during this time with increasing infection and gangrene of epidermis. Change of treatment to the wet Dakin's and saline method effected prompt healing.

Mild Conjunctivitis.—Avoid pressure from heavy compresses or tight bandages. Cold compresses of saturated boric acid constantly applied without pressure for 12 to 24 hours or longer, or hot vapor eye baths relieve the pain and discomfort, particularly the feeling of "sand in the eyes," and reduce the congestion. Personal experience leads us to recommend highly the use of a 0.5 per cent solution of dichloramine-T in chlorcosane both as a prophylactic and therapeutic measure for the ocular conditions.

Mild Respiratory Lesions.—For the mouth and throat conditions use a weak Dakin's or a .25 to .50 per cent chlorcosane solution as spray or gargle. For the aphonia use ice bag externally, and steam inhalations, with or without compound tincture of benzoin.

B. Severe Injuries.—When necrosis of the skin, more or less extensive, develops, follow the same line of treatment given above; full bath, irrigation, slush or sponge bath, or wet packs of Dakin's solution, alternating with physiologic and hypertonic salines, or the colloidal bicarbonate bath should be constantly employed. When the severe lesions are upon the shoulders, buttocks, etc., the greatest care must be taken to avoid bedsores, as they will develop very quickly. For this purpose the constant colloidal or saline bath, with patient

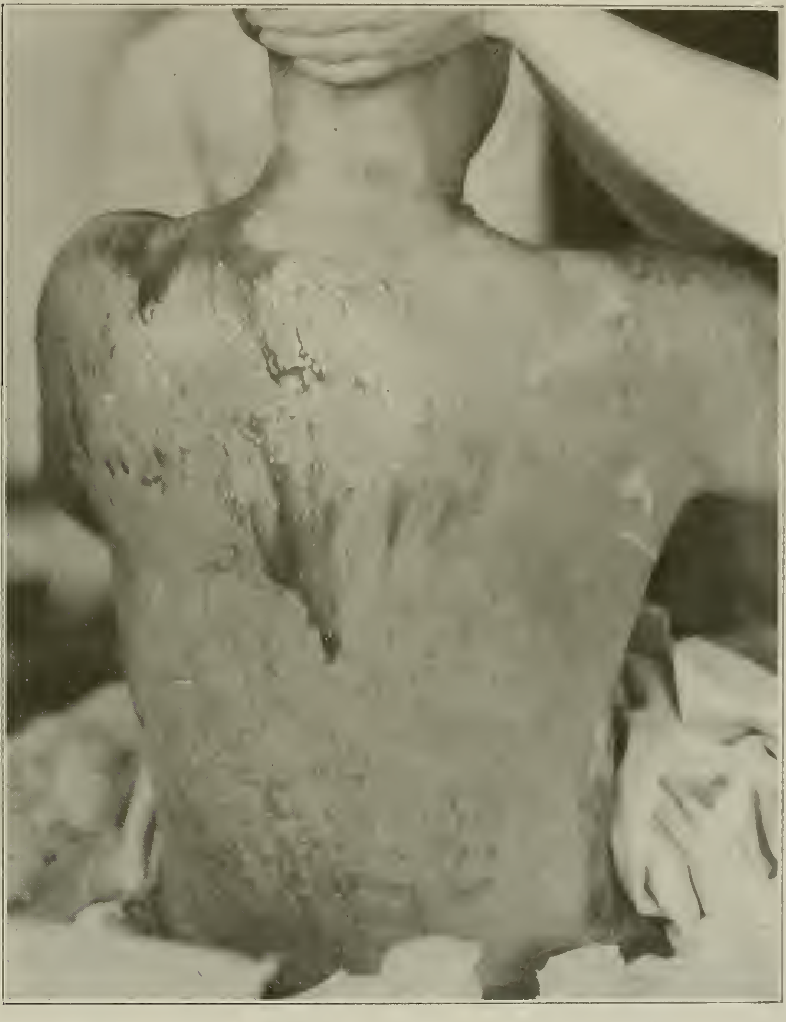

Fig. 153.—Photograph one week after three-quarters hour exposure to strong concentration of mustard gas. Treated by the grease method with resultant diffuse infection and gangrene of the skin of the back. Change to the wet Dakin's and saline methods removed the odor of gangrene at once, checked the infection and promoted prompt repair.

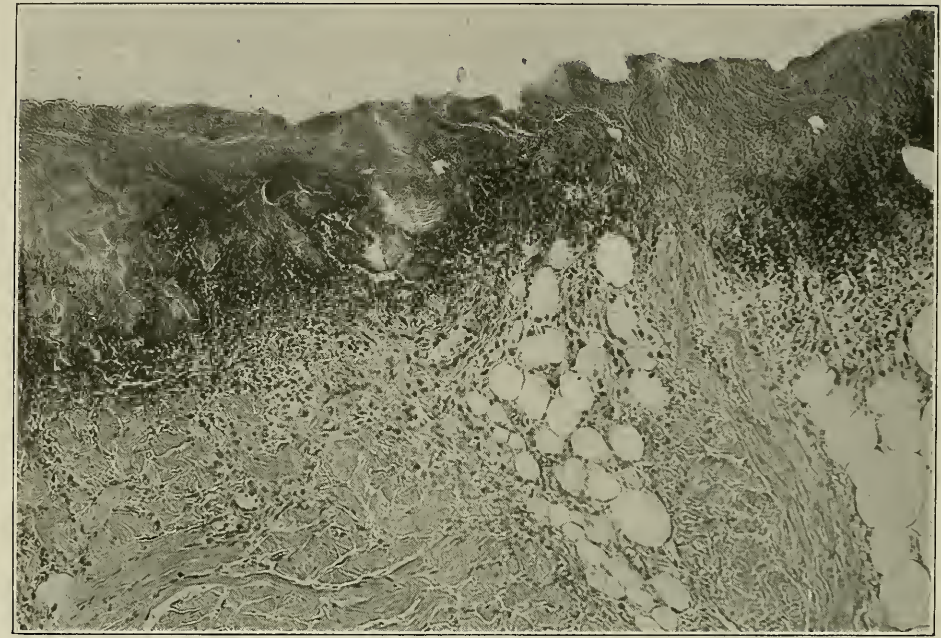

Fig. 154.—Microscopic appearance of mustard gas decubitus four weeks after exposure. Destruction of tissue too great for regeneration. Necrosis extends below the level of the sweat glands.

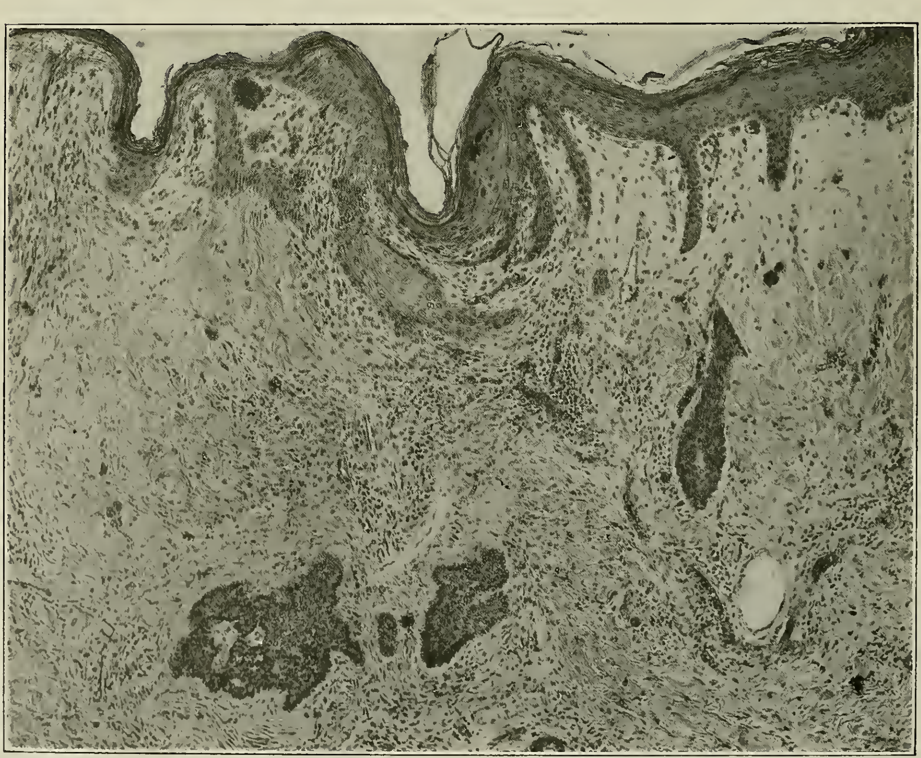

Fig. 155.—Photomicrograph of regenerating epidermis under the wet Dakin's and saline method of treatment four weeks after the injury. Note the regeneration of the epithelium from the remains of the hair follicles and sweat glands.

hung in canvas body cradle to take off pressure should be used. The cradle also gives increased facility in handling. It is of the greatest importance to protect the damaged areas from secondary trauma.

Where decubitus or sloughs occur the necrotic layer should be removed, either with sterile forceps or by means of frequent hot irrigations under pressure. For this purpose saline, Dakin's, 1:10,000 potassium permanganate solution, etc., should be used. If the necrotic areas have become infected through neglect or improper treatment, the use of Dakin's or a similar solution should be pushed, alternating with hypertonic saline baths. A hypochlorous solution made according to Carrel's method can be applied here with good results:

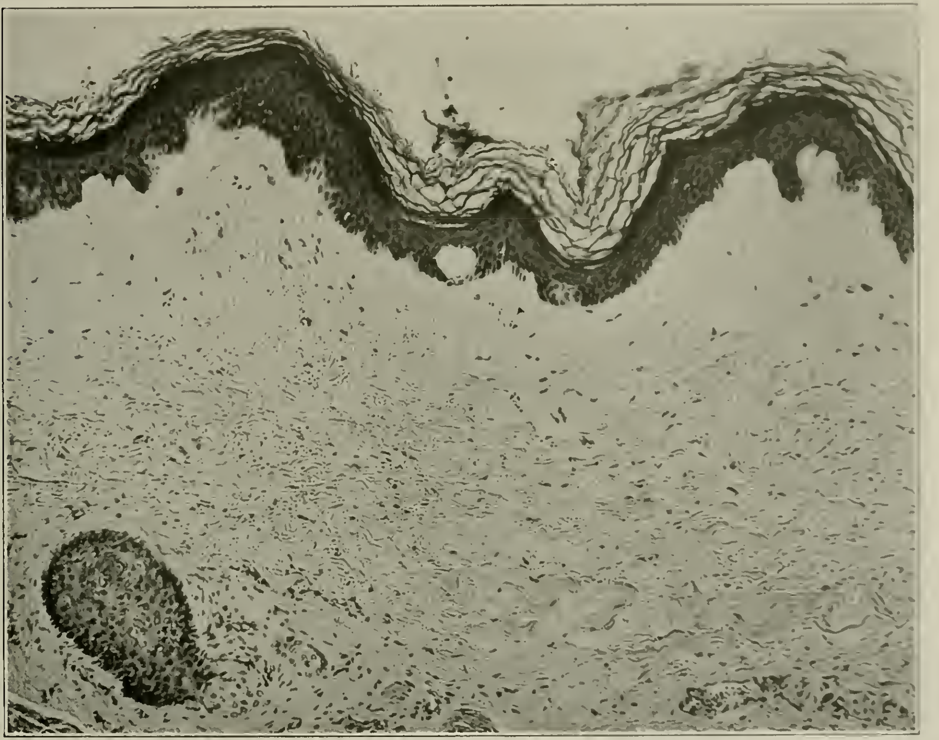

Fig. 156.—Completely healed mustard gas lesion four weeks after injury, treated twelve days with grease method with increasing infection and gangrene. Under the wet Dakin's and saline method, infection was checked promptly and healing begun. Regeneration of epidermis from hair follicles and sweat glands.

To one liter of water add 12.5 grams of bleaching powder, shake vigorously, then add 12.5 grams of boric acid powder, and shake again. Allow the mixture to stand for some hours, preferably overnight, then filter off, when the clear solution is ready for use. This solution contains about .54 per cent of hypochlorous acid, 1.28 per cent calcium biborate and .17 per cent calcium chloride. This is about the most practical concentration of hypochlorous acid, as stronger solutions rapidly lose strength.

When the patients are very weak, temperature rising, and infection progressing it may be advisable to employ tepid sponge baths of above solutions.

Complications.—*Shock* may develop immediately after the exposure but is usually not as severe as in thermal burns. Treat as in surgical shock.

Kidney.—From the time of exposure fluids should be forced to dilute the urine and lessen renal damage. When there is severe shock and excessive vomiting use Murphy drip. Use a low protein salt-free diet. When a hypertonic bath or irrigation is used great care must be taken to keep up the intake of water and prevent concentration of urine. Sodium bicarbonate may be given internally. The strengthening of the cardiac function increases the urinary output. The use of digitalis is apparently of value here, according to our experience with human cases.

Heart.—The heart rate is usually 120-140, and there is some ventricular dilatation, probably with little or no myocardial degeneration (as shown by autopsy). The use of active digitalis compounds is here indicated. (Digipuratum in doses of 1.5 grains 3 to 4 times daily seemed of benefit in our cases.)

Lungs.—For the primary bronchial and pulmonary lesions there is no specific treatment. For the secondary pneumonias (infective) proceed according to the type of infecting organism, which is likely to be the streptococcus.

Gastrointestinal.—Use liquid low protein diet. Sodium bicarbonate as indicated.

Furunculosis.—In the majority of severe dichlorethylsulphide injuries there develops about the second or third week a more or less widespread, often generalized furunculosis, usually beginning deep in the necrotic hair-follicles, and due to a staphylococcus pyogenes aureus infection. The furuncles range in size from miliary pustules to large painful boils. The large ones should be opened and drained, and a stock staphylococcus vaccine, or, if possible, an autogenous vaccine, should be given in large doses, 1 billion every third day for four injections.

Severe Eye Injuries.—Experimental evidence seems to indicate that the use of 0.5 per cent solution of dichloramine-T in chlorcosane lessens the injuries to cornea and conjunctiva, and prevents secondary infection. The use of atropine is indicated in case of involvement of the iris. The development of a chronic conjunctivitis should be prevented by the wearing of tight-fitting (but without pressure upon eyelids), antidimming goggles. The increase in refractive error or reduction of vision shown in many of the chronic irritated eyes did not respond to any treatment employed. The patient should be referred to a competent ophthalmologist for appropriate examinations and treatment for these conditions.

In the treatment of the eye lesions the use of argyrol, silvol and other silver preparations, as well as cocaine, is considered unwise. (See chapter on Ocular Lesions.)

General Toxic Action.—No evidences of a toxic action upon the internal organs have been seen in any of the lesions of mustard gas produced by direct application or by exposure to its vapor. Clinical studies, as far as carried out, show increased blood urea, decreased urea- and chloride-output, decreased quantitative urinary output, and increased specific gravity, with increased acidity. The toxic symptoms observed could be explained as the result of the skin destruction, damage to the respiratory tract, secondary infection, decubitus, with resulting absorption, etc. In the earlier stages symptoms of severe shock may be present. Treatment of these conditions should be carried out according to general principles.

SEQUELÆ.—After healing of the skin lesions a severe itching may persist for many weeks or months. This is true, even of the mildest lesions; accompanying the itching the affected part may show a branny desquamation, or secondary vesicles may develop after rubbing (Nikolsky's sign). Benzyl alcohol has been recommended for the itching.

In the case of extensive cicatrices of the skin, skin-grafting is advisable, and the patient should be told the importance of protecting such areas from injury, because of the possibility of a future development of squamous cell carcinoma in such scars, as in the case of thermal burns.

Patients with respiratory lesions due to mustard gassing should be warned of their increased susceptibility to diphtheria, influenza, bronchitis, pneumonia, and tuberculosis, and advised accordingly. Soldiers, as well as others, who have had moderate or severe respiratory symptoms due to mustard gassing, should be sent to a high, dry region, and, in general, receive the same hygienic treatment given cases of early tuberculosis. They should be regarded as having a reduced expectancy of life. Chronic bronchitis, cicatricial contractions of respiratory passages, and chronic pneumonia with pulmonary sclerosis are respiratory sequelæ demanding special forms of treatment.

CHAPTER VIII

GENERAL SUMMARY OF DICHLORETHYLSULPHIDE (MUSTARD GAS) POISONING

I. Local Action.—*Skin.*—Dichlorethylsulphide ("Mustard Gas"), in liquid or in vapor form, even in very low concentrations, is an escharotic poison for the animal tissues (skin, conjunctivæ, cornea, mucous membranes of respiratory and gastrointestinal tracts) with which it comes in direct contact. The degree of the injury is proportionate to the concentration of the gas, the time of exposure, individual susceptibility, and local physical conditions, such as moisture, sweating, warmth, pressure and friction. The escharotic action is, for the greater part, painless, the anesthetic effect being especially notable upon the skin; while upon the mucous membranes its action may be more irritant, probably chiefly reflex in character. The cutaneous surfaces most susceptible are those with thinner, more delicate skin, well supplied with sweat glands and hair follicles, where sweat may collect, and which are exposed to friction or pressure, such as the axillæ, flexor surfaces, genitals, inner surface of arms and corresponding surface of trunk, inner surfaces of thighs, between the fingers, etc. There is a penetration of the gas into the sweat and sebaceous glands, and a re-solution of mustard gas vapor in sweat and sebum occurs. The injuries are particularly striking in their insidious, slowly progressive development, becoming first apparent only some hours after the exposure. Upon human skin the lesion appears as a hyperemia, followed by vesication, eschar formation, sloughing, and slow healing, with more or less pigmentation. Depilation may occur; in severe cases the eschar may extend entirely through the corium into the subcutaneous tissues. Secondary infection and gangrene of the eschars occurs invariably in cases not properly treated. Milder lesions may show only the earlier stages of hyperemia, vesication or pigmentation. In general the injuries may be classed as burns of first, second, or third degree. Following extensive hyperemias in human skin a most marked pigmentation, exceeding in degree the most marked forms of solar tan may be quickly developed and fade slowly. The pigmentation may be diffuse or spotted. In human skin vesication is pronounced; in animals the cutaneous lesions are characterized by the development of marked subcutaneous edema in the injured area. The fluid of the vesicle or of the edema is nonirritating when applied to uninjured areas. In the case of human skin frequently exposed to very dilute concentrations (only perceptible by odor), an eczematous itching condition between the fingers, on the genitals, etc., may develop; rubbing or scratching of the itching part may lead to the quick development of a blister or superficial eschar (Nikolsky's sign). Such interdigital lesions in laboratory workers may resemble clinically those produced by the itch mite. The genital lesions may be mistaken for venereal sores. Cutaneous areas injured by mustard gas are rendered more susceptible to trauma or other forms of injury, including new exposures to mustard gas. This local susceptibility is, however, a general one, and not a specific lowered resistance to the action of dichlorethylsulphide. Subcutaneous injections of pure dichlorethylsulphide produce painless eschars, followed by dry sloughing, with edema less marked than in the case of external cutaneous application; a hypostatic edema may develop on the animal's belly when injected in the back. In the tissues at the site of the injection and in the hypostatic edema mustard gas may be present for some days after the injection as shown by odor and physiologic reaction. The resolution of mild skin injuries is often attended by troublesome itching. Healing of the deep cutaneous eschars is very slow; during the healing of extensive deep lesions the patients complain of a sensation of "tightness" or contraction of the skin; large scars may be produced resembling those resulting from deep thermal burns. The hairs may be lost; but when regenerated they may be white in color. Mild burns may be more painful than severe ones.

Eye.—Upon the cornea mustard gas exerts an especially injurious action, particularly at the vertex. Within ten to fifteen minutes after exposure to dilute concentrations, degeneration or necrosis of the corneal surface may be demonstrated by the application of a 2 per cent alkaline aqueous solution of fluorescein, the injured cells retaining a greenish fluorescent coloration. In more severe injuries the cornea may be killed throughout its entire thickness at the vertex. The mildest cases show a slight cloudiness: the severe cases present a characteristic porcelain appearance of bluish white opalescent cloudiness, often with a more opaque band or line running horizontally across the cornea just below its transverse diameter. The injury to the conjunctiva is shown by the development of a more or less severe catarrhal, seropurulent or purulent conjunctivitis with marked edema of the subconjunctival tissues leading often to "ruffling" of the lids, entropion, ectropion, or a combination of these. Even the lighter cases tend to run a chronic course with disturbances and reduction of vision. In the severe cases cicatrization and vascularization of the cornea take place slowly with resulting impairment or loss of vision. The injured eye is more susceptible to infection; and in infected cases suppurative panophthalmitis may develop with complete destruction of the eyeball. Recovered cases of mild mustard gas conjunctivitis often show an increased sensitivity to the action of light, dust, and other irritants, including mustard gas fumes.

Respiratory Tract.—Upon the mucosa of the respiratory tract mustard gas vapor produces a local injury to the epithelium as shown by the development of a catarrhal, desquamative, membranous, diphtheritic or purulent inflammation (rhinitis, stomatitis, pharyngitis, laryngitis, tracheitis and bronchitis), these lesions being most severe in the nose, back of tongue, palate, pharynx and larynx, decreasing in intensity downwards. Coryza, salivation, dryness of mouth and throat, aphonia and persistent cough are the chief symptoms, with physical signs of laryngeal, tracheal and bronchial involvement, and atelectasis, emphysema and edema of the lungs. As a result of secondary infection a purulent bronchopneumonia may develop.

Gastrointestinal Tract.—Through the swallowing of air, saliva or secretions from the upper respiratory tract containing mustard gas, or from the ingestion of contaminated food local corrosive action upon the alimentary mucosa may be produced, varying from a catarrhal inflammation to large areas of eschar formation with resulting gastric ulcer, perforation, etc. The symptomatology of the mildest lesions is covered up by that resulting from the more severe burns elsewhere; the more severe ones will produce marked symptoms referable to the stomach and intestines.

II. SUSCEPTIBILITY.—There exists a racial (whites more susceptible than negroes) and an individual susceptibility to the action of dichlorethylsulphide, particularly in the case of the skin, and probably also of the respiratory tract. The individual susceptibility, in some cases at least, is associated with the constitutional stigmata and symptomatology of the thymicolymphatic constitution. Acquired susceptibility is not specific. Animals show also generic and individual differences in sensitivity to mustard gas.

Systemic Action.—There is no evidence of any systemic poisoning by the absorption of dichlorethylsulphide from the skin, eyes or mucous membranes of the respiratory or gastrointestinal tracts. There is no metastatic action of the gas from the site of local external application.

Shock.—In all severe cases of mustard gas burns of skin, eyes, or mucous membranes there is usually the clinical picture of severe shock, in the form of intense pallor, depression of pulse and temperature, general collapse, nausea and vomiting. The mildest cases show no systemic reaction.

Blood and Urine.—No changes are observable in the blood or urine of mild cases. In cases with large infected burns of skin or respiratory tract, the blood presents a mild secondary anemia with leucocytosis; the blood urea is increased; the urine is diminished, concentrated, and contains casts and albumin. Under forced fluids the urinary symptoms improve, and the blood urea diminishes. In severe infected cases the general picture may be that of a severe toxemia. In experimental animals, after more severe gassing with involvement of the respiratory tract, there occurs a distinct concentration of the blood, with a polycythemia of two to three million above the normal, and a corresponding leucocytosis.

Intravenous and Subcutaneous Injection.—When injected intravenously or subcutaneously dichlorethylsulphide is an active poison, causing death in one to four hours intravenously and two hours to three weeks after subcutaneous injections (for rabbits intravenous injections of .0075 c.c. per kilo may be lethal within four hours), according to size of dose, individual animal, etc. When death takes place quickly, the symptoms are chiefly those of an action upon the central nervous system, such as hyperexcitability, rapid respirations, general convulsions, opisthotonos, gradual failure of respiration and circulation, coma and death. When the animal lives longer after small intravenous injections, or after subcutaneous injection, there develops a characteristic symptomatology of salivation, marked diarrhea, leucopenia, and fall of temperature, with marked anorexia, emaciation and depression. With subcutaneous injections of .015 to .06 c.c., death usually takes place from the fourth to the tenth day.

III. PATHOLOGY.—The specific microscopic pathology of the local lesions of dichlorethylsulphide poisoning consists in degeneration and necrosis of the cells with which it comes in contact. The earliest microscopic change is pyknosis of the nucleus and cell body, followed by hydropic degeneration, liquefaction or coagulation necrosis. In the skin, hyperemia, with regeneration of the damaged cells, pigmentation, vesicle formation, desquamation of the dead epidermis or eschar formation mark varying stages of severity of the lesion. The degenerative changes extend deepest in the hair follicles and sweat glands. In mild burns without vesication the papillary layer of the corium may show a greater degree of necrosis than the epidermis itself, thus explaining the frequent occurrence of Nikolsky's sign. Large, heavily pigmented chromatophores may be the only living cells left in the papillary layer. In severe burns the necrosis may extend entirely through the corium. In the cornea, pyknosis and simple or coagulation necrosis of the corneal epithelium and interstitial substance, even to the endothelial layer, in extent varying with the degree of exposure, constitute the microscopic features. On the conjunctivæ the epithelium shows pyknosis, hydropic degeneration, liquefaction necrosis, or there may be a deeper necrosis extending into the subconjunctival tissues. The conjunctival surface suffers to a less degree proportionately than the epidermis. On the mucous membranes the epithelium shows pyknosis, hydropic or mucoid degeneration, desquamation, liquefaction or coagulation necrosis. The necrosis may extend into the submucosa, but the depth of the lesions on the conjunctivæ and the mucous membranes of the respiratory tract is never so great from identical exposures, as it is in the skin. Following the necrosis there is marked hyperemia, and the development of an edema, more marked in the subcutaneous and subconjunctival tissues in animals, but less marked in man. Human skin, however, shows a much greater tendency to vesication. The blood vessels in the necrotic area are killed, the blood cells hemolyzed to some extent without thrombus formation or much extravasation, except minute hemorrhages by diapedesis. Following the lesion there is a demarcating inflammation, with slow regeneration, repair or cicatrization. The regeneration of the epidermis proceeds from the epithelium of the sweat and sebaceous glands. On the mucous membranes there results in the severe cases a localized eschar or ulcer, or a more diffuse diphtheritis. With secondary infection the inflammatory process becomes purulent or suppurative. The influence of secondary trauma and infection is well shown in the early development of deep areas of decubitus in the injured regions of the skin. Multiple furuncles may develop, or large cutaneous areas become gangrenous. In the eye purulent involvement of the anterior chamber, iris and ciliary body may occur, or even a suppurative panophthalmitis. In the respiratory tract secondary infection of the injured mucosa may lead to a purulent bronchopneumonia.

The internal organs in animals with mustard gas lesions of the skin, eyes, respiratory or gastrointestinal tract offer nothing of a specific pathologic nature. There is general congestion, marked splanchnic congestion, acute catarrh of the intestines and, in infected cases, some cloudy swelling of the kidneys.

In fatal cases the cause of death is to be found in shock, secondary infection with toxemia, or local conditions as laryngitis, tracheitis, bronchitis and bronchopneumonia. It is also possible that the entrance into the body of shell fragments carrying liquid dichlorethylsulphide might cause a relatively speedy death through absorption.

At the site of subcutaneous injections there is found a local eschar with demarcating hemorrhage, edema and inflammatory infiltration; in the large veins into which injections have been made, no changes have been found except occasional thrombosis.

The general pathology of the injected cases presents a specific pathologic picture in the intestinal tract in the form of a severe mucoid, desquamative or necrotic enteritis, the intestinal epithelium showing the most marked hydropic or mucoid degeneration, even to liquefaction necrosis. Similar changes may be found in the epithelium of the bile ducts. In a certain number of cases the spleen, lymph nodes and hemal nodes show a marked hemosiderosis, the hemosiderin being contained in large hemophages. It is most probable that these evidences of increased hemolysis are explainable by the extravasations and blood destruction occurring at the site of the injection, or are simply coincident pathology due to some other cause, as such hemosiderosis is not a rare finding in laboratory animals. Marked depletion of the bone marrow is produced by small doses intravenously. In the other organs no pathologic changes but congestion and edema have been found, with the rare exception of emboli or thrombi.

IV. Mode of Action.—The cause of death in intravenous and subcutaneous injections would appear to be the direct action of minute quantities of free dichlorethylsulphide or some poisonous product resulting from its decomposition, upon the cells of the central nervous system. It has been assumed that the pathologic action of dichlorethylsulphide is due to its hydrolysis within the tissue cells. The products of this hydrolysis, hydrochloric acid and dihydroxyethylsulphide, when injected into the blood, do not produce the same effects. Dihydroxyethylsulphide and hydrochloric acid, when injected into the circulation in much larger doses than would result from the hydrolysis of the fatal doses of mustard gas, are harmless. The effect upon the cells of the central nervous system, may, however, depend upon hydrolysis, with the liberation of hydrochloric acid (*Marshall*) in these cells, of minute quantities of mustard gas from the circulation, or these cells may be injured without such hydrolysis occurring. It is probable that the gastrointestinal catarrh resulting from the injections of dichlorethylsulphide is secondary to the nervous injury, rather than to an excretion of the poison or poisonous products through this tract although this point remains unsettled. No positive tests for dichlorethylsulphide or dihydroxyethylsulphide have been obtained in the bile, intestinal contents, or urine. We have, therefore, failed to confirm *Marshall's* statement that dihydroxyethylsulphide is excreted in the urine in mustard gas poisoning. Incidentally, it has been shown that the platinic chloride-sodium iodide color test for dichlorethylsulphide is not applicable to the body fluids or extracts of various organs and tissues, as similar color changes are produced by some of these.

V. Treatment.—The principles of treatment to be applied to mustard gas injuries are primarily those that will remove any of the gas remaining, lessen necrosis, prevent infection, and promote healing. Our experience leads us to recommend the use of Dakin's solution in irrigation or full baths for the skin lesions, and a 0.5 per cent solution of dichloramine-T for the eye lesions, and also as a mouth wash. The fluid intake should be forced when the urine is concentrated. Pressure must be removed from all injured areas. Air-excluding and infection-including protections, such as oily dressings, paraffin sprays and coatings, zinc stearate, olive oil, vaseline, etc., should not be used, unless there is an active and persistent germicidal agent present as in the case of sodium stearate impregnated with chloramine-T, or the chlorcosane solution of dichloramine-T.

The respiratory lesions can be treated only symptomatically.

VI. Sequelæ.—Among the most important sequelæ of mustard gassing is the apparent increased susceptibility to diphtheria, influenza, bronchitis, pneumonia and tuberculosis following lesions of the respiratory tract. The respiratory infections may become chronic and death from these may take place months after the gassing. Persistent aphonia, due to local lesions, or as one expression of a traumatic neurosis, is not a rare sequel. Chronic disturbances of vision are also in part the result of local changes, and in part psychical. In the skin, conditions of chronic eczema, smarting, burning, itching and desquamative dermatitis, and pigmentation occur as sequelæ. Leucotrichia has also been observed. It is safe to predict that a development of squamous-celled carcinoma in the extensive cicatrices following mustard gas lesions may take place 15 to 25 years later, as in the case of extensive thermal burns. Finally, the importance of the psychical disturbances following mustard gassing should not be minimized.

VII. As to its use in warfare, mustard gas is a disabling rather than a killing agent. Under the actual conditions of the field the great majority of mustard gas casualties are likely to be of a nature tending to incapacitate the injured for service for a number of days or weeks, or even for months. Added to this, the insidious character of this invisible fire, painless and often unrecognized in its action, makes mustard gas a potent factor in undermining the morale of the troops exposed to it.

Finally, from the experience of the last several months, it is evident that the soldier who has suffered respiratory mustard gassing loses in expectancy of life from the standpoint of vital insurance through the possibility of development of cicatricial contractions and chronic processes in the respiratory tract.

APPENDIX: Experiments recently conducted by us indicate that different solvents of mustard gas alter its action in varying degrees. Alcoholic solutions produce burns characterized by consecutive crops of vesicles, marked Nikolsky's sign, and greater pain and itching.

BIBLIOGRAPHY

A. Medical Aspects of Dichlorethylsulphide Gassing

1. Meyer, Victor: Ber. d. deutsch., chem. Gesellsch., 1886, xix, No. 3, p. 3259.
2. —: Ber. d. deutsch. chem. Gesellsch., 1887, xx, No. 2, p. 1729.
3. Giraud: Les premiers symptômes de l'intoxication par les gaz moutarde, Jour. de méd. et de chir. prat., 1917, lxxxviii, 890-894; Abst. in Med. Rec., New York, 1918, xciii, 21.
4. Mandel, M. and Gibson, W. S..: Clinical Manifestations and Treatment of Gas Poisoning, Jour. Am. Med. Assn., 1917, lxix, 1970-1971.
5. Teulières and Valois: Action des gaz délétères asphyxiants ou lachrymogènes sur l'appareil de la vision, Arch. d'opht., 1916-1917, xxxv, 403-410.
6. Teulières, M.: Action des gaz asphyxiants sur l' appareil de la vision, Jour. de méd. de Bordeaux, 1917, lxvi, 247-253; Abst. in Med. Rec., New York, 1917, xcii, 1077.
7. Andreoli, I.: Un caso di intossicamento da ''yprite,'' Gazz. med. lomb., Milano, 1918. lxxvii, 108-110.
8. —: [Mustard Gas on Italian Front] Gazz. d. osp., 1918, xxxix, 307; Abst. in Jour. Am. Med. Assn., 1918, lxxi, 75.
9. Amantea, G.: [Silver Nitrate Neutralizes Mustard Gas.] Policlinico, Roma, 1918, xxv, 893-895; Abst. in Jour. Am. Med. Assn., 1918, lxxi, 1781.
10. Bandaline, J. and de Poliakoff, J.: Douches d'air chaud contre les brûlures par l'ypérite, Bull. de l'Acad. de méd., Paris, 1918, lxxx, 30, 31.
11. Canelli, A. F.: Contributo alla conoscenza dell' intossicazione acuta da ''yprite'' ed in particulare del suo reperto anatomo-patologica, Riv. ospedal, Roma, 1918, viii, 2-7.
12. Cortini, A.: Circa gli effetti morbosi dell' yprite, Gior. di med. mil., Roma, 1918, lxvi, 235-243.
13. Derby, George S.: Effects of ''Mustard Gas'' on the Eyes, Am. Jour. Med. Sc., 1918, clvi, 733-736.
14. Frescoln, L. D.: Mustard (Yellow Cross) Burns, Jour. Am. Med. Assn., 1918, lxxi, 1911-12.
15. Karsner: Necropsy Service in a Military Hospital in the Field, Am. Jour. Med. Sc., 1918, clv, 904.
16. Lustig, A.: Sugli effetti del solfuro di etile biclorurato (gas vescicatorio od yprite), Sperimentale, Fierenze, 1918, lxxii, 119-128.
17. Mackenzie, G. M.: Plates Illustrating the Pathological Effects Produced by Some of the Better Known Poison Gases used by the Germans, U. S. Nav. Med. Bull., 1918, xii, 173-183.
18. Lynch, V., Smith, F. W., and Marshall, E. K.: Dichlorethylsulphide (Mustard Gas): 1. Systemic Effects and Mechanism of Action, Jour. of Pharm. and Exp. Ther., Baltimore, 1918, xii, 265-291; Abst. in Jour. Am. Med. Assn., 1919, lxxii, 680.
19. Marshall, E. K., Jr., Lynch, V., and Smith, F. W.: Dichlorethylsulphide (Mustard Gas): 2. Variations in Susceptibility of Skin to Dichlorethylsulphide, Jour. of Pharm. and Exp. Ther., Baltimore, 1918, xii, 291.
20. McDonagh, J. E. R.: The Treatment of Mustard Gas Poisoning, Med. Press, London, 1918, n.s., cvi, 365.
21. Pisarello, C.: Relazione sugli effetti morbosi delle granate cariche ad ''yprite,'' Gior. di med. mil., 1918, lxvi, 128-134.
22. Rendu, Robert: Lésions des voies respiratoires supérieures dues aux nouveaux gaz vésicants allemands, Lyon Méd., 1918, cxxvii, 108-116; Abst. in Jour. Am. Med. Assn., 1918, lxx. 1507.
23. Teulières, M.: Lésions oculo-palpébrale par nouveaux gaz., Jour. de méd. de Bordeaux, 1918, xlviii, 37-39.
24. Viale, G.: [Silver Nitrate for Mustard Gas Lesions] Policlinico, Roma, 1918, xxv, 1061, Abst. in Jour. Am. Med. Assn., 1917, lxxii, 151.
25. Editorial: The Pathology of Mustard Gas, Jour. Am. Med. Assn., 1918, xx, 1947.
26. Boxwell, W.: Poisoning by Mustard Gas; Pathological Changes, Dublin Med. Jour., 1919, cxlvii, 7-14.
27. Krumbhaar, E. B.:Rôle of the Blood and the Bone Marrow in Certain Forms of Gas Poisoning, 1. Peripheral Blood Changes and Their Significance, Jour. Am. Med. Assn., 1919, lxxii, 39-41.
28. Moorhead, T. G.: Poisoning by Mustard Gas; Clinical Results, Dublin Med. Jour. 1919, cxlvii, 1-7.
29. Pappenheimer, A. M.: The Effects of Intravenous Injections of Dichlorethylsulphide in Rabbits with Special Reference to the Blood and Haemato-poietic Tissues, Soc. Exp. Biol. and Med., (Meeting of March 19), 1919.

30. Silvan, C.: Gangrene from Gassing, Riforma Med., 1919, xxxv, 28-30; Abst. in Jour. Am. Med. Assn., 1919, lxxii, 903.
31. Editorial: Mustard Gas: Its Brief but Inglorious Career, Lancet, London, 1919, i, 471-472.
32. Great Britain: Medical Research Committee, Reports.
33. United States: Medical Advisory Board, Chemical Warfare Service, Reports.
34. Covey, G. W., and Barron, M.: Pathology of (Mustard?) Gas Inhalation, Am. Jour. Med. Sc., 1919, clvii, 808-826.
35. Gougerot and Clara: Ypérites génitales simulant la syphilis et syphilis masquée par ypérite, Ann. des Mal. Véneriennes, 1919, xiv, 257-262.
36. Lillie, R. S., Clowes, G. H. A., and Chambers, R.: Preliminary Report of Experiments on the Action of Dichlorethylsulphide (Mustard Gas) on the Cells of Marine Organisms, Science, 1919, xlix, 382.
37. Loeper: La sclérose pulmonaire consécutive à l' intoxication par l' ypérite, Prog. méd., 1919, 89.
38. Rousseau and Devaux: [Oxygen for Burns from Mustard Gassing.] Jour. de Méd. de Bord., 1919, xc, 149.
39. Ryland, A.: Laryngeal Changes Induced by Mustard Gas. Jour. of Laryng., Rhin., and Oto., London, 1919, xxxiv, 153.
40. Sollmann, T.: Dichlorethylsulphide ("Mustard Gas"). I. Influence of Solvents, Adsorbents and Chemical Antidotes on Severity of Human Skin Lesions, Jour. Pharm and Exper. Therap., 1919, xii, 303-319.
41. —: Dichlorethylsulphide ("Mustard Gas"). II. Question of Induced Hypersusceptibility of Skin, Jour. Pharm. and Exper. Therap., 1919, xii, 319-323.
42. Hopkins, E. F.: Dichlorethylsulphide ("Mustard Gas"). III. Solubility and Hydrolysis; New Method for Estimating Small Amounts, Jour. of Pharm. and Exper. Therap., 1919, xii, 393-405.
43. Smith, H. W., Clowes, G. H. A., and Marshall, E. K.: Dichlorethylsulphide ("Mustard Gas") IV. Mechanism of Absorption by Skin, Jour. Pharm. and Exper. Therap., 1919, xiii, 1-31.
44. Warthin, Aldred S., and Weller, Carl V.: The Pathology of the Skin Lesions Produced by Mustard Gas (Dichlorethylsulphide), Jour. Lab. and Clin. Med., 1918, iii, 447-479.
45. Warthin, Aldred S., Weller, Carl V., and Herrmann, George R.: The Ocular Lesions Produced by Dichlorethylsulphide ("Mustard Gas"), Jour. Lab. and Clin. Med., 1918, iv, 783-833.
46. Warthin, Aldred S. and Weller, Carl V.: The Lesions of the Respiratory and Gastrointestinal Tracts Produced by Mustard Gas (Dichlorethylsulphide), Jour. Lab. and Clin. Med., 1919, iv, 229-265.
47. Warthin, Aldred S., and Weller, Carl V.: The General Pathology of Mustard Gas (Dichlorēthylsulphide) Poisoning, Jour. Lab. and Clin. Med., 1919, iv, 265-307.
48. Herrmann, George R.: The Clinical Pathology of Mustard Gas (Dichlorethylsulphide) Poisoning, Jour. Lab. and Clin. Med., 1918, iv, 1-31.
49. Warthin, Aldred S., Weller, Carl V., Roos, Lester, and Herrmann, George R.: The Treatment of Dichlorethylsulphide ("Mustard Gas") Poisoning, Jour. Lab. and Clin. Med., 1918, iv, 833-849.

B. Medical Aspects of Gassing

(For articles dealing especially with Dichlorethylsulphide, see Section A of this bibliography.)

1914

1. Trémolières, F. and Loew, P.: Effets des gaz irritants des projectiles de guerre. Bull. et mém. Soc. méd. d. hôp. de Paris, 1914, 3.s., xxxix, 597-600.

1915

2. Achard, C.: Sur l'asphyxie par les gaz toxiques des projectiles de guerre, Bull. de l'Acad. de méd., Paris, 1915, 3.s., lxxiii, 628-631.
3. Aitchison, T.: Gas Poisoning, Brit. Med. Jour., 1915, ii, 488.
4. Bieloff N. A.: [Poisoning with German Asphyxiating Gases.] Russk. Vrach, 1915, xiv, 730-732.
5. Black, J. E., Glenny, E. T., McNee, J. W.: Observations on Six Hundred and Eighty-five Cases of Poisoning by Noxious Gases Used by the Enemy, Jour. Roy. Army Med. Corps. Lond., 1915, xxiv, 509-518; also: Brit. Med. Jour., 1915, ii, 165.
6. Bradford, J. R. and Elliott, T. R.: Cases of Gas Poisoning Among the British Troops in Flanders, Brit. Jour. Surg., Bristol, 1915-16, iii, 234-246.
7. Bramwell, W.: Poultices and Venesection in Gas Poisoning, Brit. Med. Jour., 1915, ii, 460.
8. Broadbent, Walter: Some Results of German Gas Poisoning, Brit. Med. Jour., 1915, ii, 247.

9. Campbell, H.: Poisonous Gases. Brit. Med. Jour., 1915, i, 1065.
10. Cow, D.: The Effect of Atropine in "Gassed" Patients, Lancet, London, 1915, i, 1259.
11. Cow, D. and Symes, W. L.: Treatment of the Symptoms Arising from Inhalation of Irritant Gases and Vapours, Brit. Med., Jour. 1915, ii, 76.
12. Devéze and Orsand: Masque contra les vapeurs asphyxiantes, Presse méd., 1915, xxiii, 176.
13. Dujarric de la Rivière, R., and Leclerq, J.: Étude clinique, anatomopathologique et histochimique de cas d'intoxication par les gas irritants par les Allemands à Langhemarck. Bull. de l'Acad. de méd., Paris, 1915, 3.s., lxxiii, 574-576; also: Presse méd., 1915, xxiii, 253-255; also: Med. Press and Circular, 1915, n.s., c., 362-365.
14. Dujarric de la Rivière, R. D. and Leclerq, J.: Lecture on the Effects of the Gases Employed by the Germans, Canada Lancet, Toronto, 1915, xlix, 156-166.
15. Ferrero di Cavallerleone, L.: Gas asfissianti e maschere protettive, Gior. d. r. Accad. di. med. di. Torino, 1915, 4.s., xxi, 356-370; also: Riforma med. 1916, xxii, 441.
16. Finch, G.: A Case of Optic Neuritis Following on "Gassing," Lancet, London, 1915, ii, 1027.
17. Freise: Ueber Vergiftung durch Pulvergase, Med. Klin., 1915, xi, 495.
18. Gardner, W. T.: An Inclined Plane for the Treatment of "Gassed" Cases, Lancet, London, 1915, ii, 78.
19. Giroux, L.: Hémiplégie consécutive à une intoxication par les gaz asphyxiants, Bull. et mém. Soc. méd. d. hôp. de Paris, 1915-16, 3.s., xl, 1486-1488.
20. Golla, F. and Symes, W. L.: The Immediate Effects of the Inhalation of Chlorine Gas, Brit. Med. Jour., 1915, ii, 348.
21. Hake, H. W.: The Action of Chlorine on the Blood. (Preliminary note), Lancet, London, 1915, ii, 86.
22. Heitz, J.: Sur les troubles cardiovasculaires et l'état du sang dans les intoxications par les gaz asphyxiants des Allemands, Arch. d. mal. du coeur, etc., 1915, viii, 477-454.
23. Hendry, A. W. and Horsburgh, E. L.: Some General Notes on Suffocation by Poisonous Gases with Detailed Notes on One Fatal Case, Brit. Med. Jour., 1915, i, 964.
24. Henry, H.: Notes on Postmortem Findings in Sixteen Cases of Gassing, Brit. Jour. of Surg., 1915-16, iii, 244-246.
25. Herlitzka, A.: Sulla difesa dai gas asfissianti, Gior. d.r. Accad. di. med. di Torino, 1915, 4.s., xxi, 277-304.
26. Hill, L.: Gas Poisoning, Brit. Med. Jour., 1915, ii, 801-804; also: Lancet, London, 1915, ii, 1248; also: Jour. Roy. Army Med. Corps, Lond., 1916, xxvi, 110-121; also: Tr. Med. Soc., London, 1915-16, xxxix, 102-120.
27. Hiltmann, E.: Ueber Vergiftungen durch Nitrosegase, Vrtljschr. f. gerichtl. Med., 1915, 3. F., L. 60-72.
28. Horwood, J. G.: The Prevention of Gas Poisoning, Brit. Med. Jour., 1915, ii, 161.
29. Ilyin, A. V.: [Symptomatology of Disturbances in the Nervous System in Poisoning with Asphyxiating Gases.] Psikhiat. Gaz., Petrograd, 1915, ii, 272-275.
30. Jackson, D. E.: The Pharmacological Action of Chlorine Gas, Jour. Lab. and Clin. Med., St. Louis, 1915-16, i, 447-453.
31. Kohn-Abrest, E.: Dispositif pour l'essai des substances employées contre les gaz nocifs, Compt. rend. Acad. d. sc., 1915, clxi, 310-313.
32. Kolosoff, G. A.: [Symptoms and Treatment of Poisoning with Asphyxiating Gases] Russk. Vrach, 1915, xiv, 1065-1071.
33. Leslie. R. M.: Clinical Effects of Asphyxiating War Gases, Am. Med., Burlington, Vt., 1915, x, 875-882.
34. —: Asphyxiating Gases in War, Brit. Jour. Nursing, 1915, lv, 3; also: Midland Med. Jour., Birmingham, 1915, xiv, 115.
35. Lévy, F.: Étude sur le syndrome respiratoire consecutive à l'absorption de gaz asphyxiante, Presse méd., 1915, xxiii, 255; also: Med. Press and Circular, 1915, n.s., c, 384-386.
36. Lervin, L.: Ueber Vergiftung durch kohlenoxydhaltige Explosionsgase aus Geschossen, München med. Wchnschr., 1915, lxii, 465.
37. Lian, C.: Les intoxiqués par les gaz asphyxiants au poste de secours, Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, 3.s., xxxix, 1067-1072.
38. Loeper, Peytel and Sabadini: La gastrite des soldats asphyxiés, Presse méd., 1915, xxiii, 240; also: Med. Press and Circular, 1915, n.s., C, 188-190.
39. Lung, G. A.: Asphyxiating Gases as a Weapon in Warfare, Mil. Surgeon, Chi., 1915, xxxvii, 411-424.
40. McCullough, J. W. S.: Poisoning by Noxious Gases, Canad. Pract. and Rev. 1915, xl, 525-531.
41. McIntire, J. T.: Asphyxiating Gases, Jour. Roy. Army Med. Corps, Lond., 1915, xxiv, 302.
42. McWalter, J. C.: Dry-land Drowning (Gas Poisoning), Med. Press and Circular, 1915, n.s., C, 303.
43. —: The Prevention of Gas Poisoning, Brit. Med. Jour., Lond., 1915, ii, 118.
44. Mortimer, J. D.: The Treatment of Gas Poisoning, Lancet, London, 1915, i, 1262; also: Med. Press and Circular, 1915, n.s., xcix, 566.

45. Nikolsky, D.: [Construction of a Museum of Devices against the Action of Asphyxiating Gases] Russk. Vrach, 1915, xiv, 738.
46. Parker, R.: Poisonous Gases, Brit. Med. Jour., 1915, i, 1027.
47. Pellegrini, R.: Studi sui gas asfissianti; l'azione dei vapori di bromo sui lipoidi surrenali e sulle cellule cromaffini. Riv. di med. leg., Pisa., 1915, vi, 313-320.
48. Pieri, G.: L'intossicazione da gas asfissianti (chloro), Riv. ospedal., Roma, 1915, v, 542-549.
49. Pozhariski, I. F.: [Pathological-Anatomical Alterations in the Bodies of those Dead from Asphyxiating Gases.] Russk. Vrach, 1915, xiv, 673-677; Abst. in Jour. Am. Med. Assn., 1915, lxv, 1496.
50. Rathery, F. and Michel, R.: Les accidents occasionnés par les gas toxique dits asphyxiants employés par les allemands; étude de clinique, anatomo-pathologique et thérapeutique, Paris méd., 1915-16, xvii, 389-394; Abst. in La Riforma Medica, 1916, xxii, 101.
51. Roberts, A. A.: The Poison War, William Heinemann, London, 1915, p. 144. Review in Brit. Med. Jour., 1915, ii, 15.
52. Sadovski P. P.: [Poisoning with Asphyxiating Gases en masse.] Sibirsk. Vrach, Tomsk, 1915, ii, 189-191.
53. Schäfer, Sir Edward.: On the Immediate Effects of the Inhalation of Chlorine Gas Brit. Med. Jour., 1915, ii, 245.
54. Sergent, E. and Agnel A.: Note sur quelques effets cliniques des gaz asphyxiants. Bull. et mém. Soc. méd. d. hôp. de Paris, 1915, 3. s., xxxix, 960-964; also: Bull. med., Paris, 1915, xxix, 6.
55. Serono, C. and Trocello, E.: I gas asfissianti e tossici adoperati in guerra e la difesa contro di essi, Arch. di farmacog., etc., Roma, 1915, iv, 167-174.
56. Serono, C. and Trocello, E.: Sulla difesa dai gas asfissianti, Annali di medicina navale e coloniale, May, 1915; Abst. in Annali D'Igiene, 1916, xxvi, 56.
57. Skvortsoff, V. I.: [Treatment of those Poisoned with Asphyxiating Gases.] Russk. Vrach. 1915, xiv, 793.
58. Symes, W. L.: Notes on the Treatment of the Symptoms Arising from Inhalation of Irritant Gases and Vapors, Brit. Med. Jour., 1915, ii, 12.
59. Symes, W. L. and Golla, F. L.: Note on the Bronchiolar Obstruction Set up by Irritant Vapor and its Relief by Atropine, Jour. Physiol., 1915, xlix, p. LV.
60. Tengeley, Ida, C.: The Use of Atropine in Gassed Patients, Lancet, London, 1915, i, 1203.
61. Tilden, W. A.: Poisonous Gases in Warfare and their Antidotes, Nature, London, 1915, xcv, 395-397.
62. Vershinin, N. V.: [Poisoning with Asphyxiating Gases.] Sibirsk. Vrach, Tomsk, 1915, ii, 231.
63. Vishegorodskaya, Ye. S.: [Cases of Nervous Disturbances in Poisoning with German Asphyxiating Gases.] Psikhiat. gaz., Petrograd, 1915, ii, 275.
64. Wainwright, L.: What is the Gas? Lancet, London, 1915, ii, 198.
65. Watt, A. H. and Irvine, L. G.: Treatment of Gas Poisoning in Transvaal Mines. Brit. Med. Jour., 1915, ii, 247.
66. Yablonski, Ye. R.: [Apparatus for Giving Aid to those Poisoned with Gases, or Found in a State of Asphyxia.] Morsk. Vrach, Petrograd, 1915, 280-296.
67. Editorial: The German use of Asphyxiating Gases, Brit. Med. Jour., 1915, i, 774, 821, 861, 984, 1016.
68. Editorial: Le chlore gaz asphyxiant Presse méd. 1915, xxiii, 185, 186.
69. Editorial: Les gaz asphyxiants, Rev. gén. de clin. et de thérap., 1915, xxix, 476-477.

1916

70. Ascoli, M.: Note cliniche sull' avvelenamento da gas asfissianti, Riv. ospedal., Roma, 1916, vi, 792-798; also: Med. nuova, Roma, 1917, viii, 41-44.
71. Bigg, E.: Notes on Three Cases of Chlorine Gas Poisoning, Lancet, London, 1916, ii, 341.
72. Bilancioni, G.: Alterazioni anatomiche delle prime vie aeree e digerenti da gas asfissianti, Arch. ital. di laringol., Napoli, 1916, xxxvi, 143-169; also: Arch di farm. sper., Roma, 1917, xxiii, 3-30; Abst. in Brit. Med. Jour., 1917, i, 90 D.
73. Boudreau, L.: L'iode et les gaz asphyxiants, Jour. de méd. de Bordeaux, 1916, xlvi, 214-217.
74. Businco, A.: I gas cosi detti asfissianti in guerra, Riv. di med. leg., Pisa, 1916, vi, 305-312, 337-343.
75. Carpenter, D. N.: Smoke and Powder Gases in Naval Warfare, Mil. Surgeon, 1916, xxxix, 461.
76. Cevidalli, A.: Asphyxies et gaz asphyxiants; moyens d'y remédier. Paris, 1916, H. Dunod et E. Pinat, 72, p. 80. Review in Riforma med. 1916, xxxii, 1210-1212.
77. Chassevant, A.: Traitement des victims des gaz asphyxiants. Bull. gén. de thérap., [etc.]. 1916-17, clxix, 29-31.
78. Chugunoff, S. A.: [Disturbances on the Part of the Nervous and Mental System After Intoxication with the Poisonous Gases Used by the Germans.] Voyenno. Med. Jour., Petrograd, 1916, ccxlv, med. spec. pt., 222-240.

79. Cormio, R.: Note cliniche e terepeutiche sull' avvelenamento da gas asfissianti, Policlinico, 1916, xxiii, 1231-1234; also: Gazz. med. lomb., Milano, 1917, lxxvi, 52-55; also: Gazz. med. sicil., Catania, 1917, xx, 145-154.

80. Crabbe: Report on Postmortem Examination of E. R., aged 21, German Prisoner of War (Gas Poisoning), Jour. Roy. Army Med. Corps, Lond., 1916, xxvi, 240.

81. D.R., N.: Gas asfissianti e iniezioni endovenose de ossigeno, Malat. de Cuore, Roma, 1916-17, i, 435.

82. Elliott, J. H. and Tovell, H. M.: The Effects of Poisonous Gases as Observed in Returning Soldiers, Internat. Jour. Surg., 1916, xxix, 383-388.

83. Elliot, T. R. and Henry, H.: Gas in Military Mines, Symptoms of Carbon Monoxide Poisoning, Hospital, London, 1916, lx, 169.

84. Filippini, A.: La difesa contro i gas asfissianti, Ann. d'ig. sper. Roma, 1916, xxvi, 705-713.

85. Franco, P. M.: Intossicazioni per gas asfissianti, Studium, Napoli, 1916, ix, 40.

86. Gallo, G.: Osservazioni cliniche su ottantadue casi di intossicazione da gas asfissianti in guerra, Gior. di med. mil., Roma, 1916, lxiv, 772-804; also: Riforma Med. Naples, 1917, xxxiii, 100-104; abst. in Mil. Surgeon, 1917, xl, 578.

87. Giordano, M.: [Poisoning by Arseniuretted Hydrogen on Submarines.] Ann. di med. nav., Roma, 1916, ii, 319-329; also; U. S. Nav. Med. Bull., 1917, xi, 342-346.

88. Grémeaux, P.: Lésions oculaires consécutives à l'action des gaz lacrymogènes, Chin. opht., Paris, 1915-16, xxi, 609-612; Progrès méd., 1916, 3.s., xxxi, 157.

89. Hebblethwaite, A. S.: Treatment of Chlorine Gas Poisoning by Venesection, Brit. Med. Jour., 1916, ii, 107.

90. Irvine, L. G.: Gassing Accidents from the Fumes of Explosives, Brit. Med. Jour., 1916, i, 162-166.

91. Lucherini, T.: A proposito dei gas asfissianti, Arch. di farmacol. sper., Roma, 1916, xxii, 429-441; also: Gazz. med. lombarda, Milano, 1917, lxxvi, 13-18.

92. McWalter, J. C.: Gas Poisoning, Clin. Jour., Lond., 1916, xlv, 172-174.

93. Ménétrier and Martinez: Tuberculose pulmonaire consécutive à l'inhalation de gaz asphyxiants, Rev. gén. de. clin. et de thérap., 1916, xxx, 462.

94. Obnesorg, K.: Intoxication by Detonation and Explosion Gases Aboard Ship, U. S. Nav. Med. Bull., 1916, x, 625-633.

95. Pellegrini, R.: Sui gaz asfissianti usati in guerra; considerazioni ed osservazioni personali, Pensiero med., Milano, 1916, vi, 493, 505, 517.

96. —: Sulle lesioni anatomopatologiche da gaz asfissianti, Morgagni, Milano, 1916, lviii, pt. 1, pp. 297-309.

97. Pisano, G.: Contributo alla conoscenza dell azione tossica dei gas velenosi usati dagli Austro-Tedeschi, Gazz. d. osp., 1916, xxxvii, 1521.

98. Rabena, F., Los gases asfixiantes como arma de la presente guerra europea, Rev. valenc. de cien. med., Valencia, 1916, xviii, 113.

99. Rho, F.: Avvelenamento per gas derivanti dagli esplosivi sulle navi da guerra, Ann. di med. nav., Roma, 1916, ii, 336-343.

100. Richards, E. T. F.: Gas Poisoning: Observations during a medical Service with the British Expeditionary Force in France, St. Paul Med. Jour, 1916, xviii, 153-157.

101. Sisto: L'avvelenamento per gas asfissianti, Riforma med., 1916, xxxii, 1234, 1265, 1290.

102. Sundell, C.E.: The Clinical Manifestations of Gas in Military Mines. Lancet, London, 1916, i, 957; also: Jour. Roy. Army Med. Corps, Lond., 1917, xxviii, 725-727.

103. Symons, C. H.: Poisoning by Gases from Explosives, Jour. Roy. Med. Service, Lond., 1916, ii, 513-516.

104. Teynac, A.: Sur un cas d'asphyxie multiple et compliquée observé sur le front, (etc.); Jour. de Méd. de Bordeaux, 1916, xlvi, 107-111.

105. White, W. H.: The Treatment of Chlorine Gas Poisoning by Venesection, Brit. Med. Jour., 1916, ii, 159.

106. Zadek, Jr.: Massenvergiftung durch Einatmung salpetrigsamer Dämpfe (Nitritintoxikationen), Deutsch. med. Wchnschr., 1916, xliii, 208; also: Berl. klin. Wchnschr., 1916, iii, 246-250.

107. Editorial: Gas in Military Mines: the Symptoms of Carbon Monoxide Poisoning, Hospital, London, 1916, lx, 169.

108. —: I gas asfissianti in guerra; impiego ed effeti; difese e provvedimenti, Riv. d'ig. e san. pubb., 1916, xxvii, 409-420.

1917.

109. Achard, C., Flandin, C. and Desbouis, G.: Mesure de l'intoxication oxycarbonée par la capacité respiratoire du sang; contrôle de traitement par les inhalation d'oxygene, Compt. rend. Soc. de biol., 1917, lxxx, 397-401.

110. Achard, C. and Flandin, C.: A propos de la mesure de l'intoxication oxycarbonée par la capacité respiratoire du sang, Compt. rend. Soc. de biol., 1917, lxxx, 698-700.

111. Agasse-Lafont, E. and Roux, J. C.: [Stomach Disturbances in the Gassed.] Arch. des Mal. de l'Appareil Digestif, etc., 1917, ix, 341; Abst. in Jour. Am. Med. Assn., 1917, lxix, 2211.

112. Boldireff, V. N.: [Treatment of Poisoning from Asphyxiating Gases.] Russk. Vrach, 1917, lxix. 390; abst. in Jour. Am. Med. Assn., 1917, lxix, 2007.
113. Colard and Speil: A propos de l'intoxication par les gaz asphyxiants et son traitement, Archives Médicales Belges, Paris, 1917, lxx, 577; Abst. in Jour. Am. Med. Assn., 1917, lxix, 1203.
114. DeDominicis, A.: Sulle iperasfissie da idrogeno solforato ed acido cianidrico, Cesalpino, Arezzo, 1917, xiii, 37-39.
115. —: È giustificato il concetto di iperasifissia od asfissia da ossido di carbonio? Cesalpino, Arezzo, 1917, xiii, 113-115.
116. Fiessinger, C.: Les accidents cardiaques par les nouveaux gaz asphyxiants, Bull. de l'Acad. de Méd., Paris, 1917, lxxviii, 322-328. Rev. gén. de clin. et de thérap., 1917, xxxi, 617-619; also: Gazz. med. lomb., Milano, 1918, lxxvii, 25-27; Abst. in Jour. Am. Med. Assn., 1917, lxix, 1832.
117. Foy, G.: Poisonous Gas, Med. Press and Circular, 1917, n.s., ciii, 16.
118. Gakh, K. F.: [Intravenous Injections of Oxygen in Treatment of Poisoning from Asphyxiating Gases.] Russk. Vrach, 1917, xvi, 403; Abst. in Jour. Am. Med. Assn., 1917, lxix, 2007.
119. Gaussorgues, M.: Causerie sur les gaz asphyxiants, Montpellier Méd. 1917, xxxix, 1075-1087.
120. Gimbert: Action provocatrice des gaz asphyxiants sur la tuberculose pulmonaire, Presse méd., 1917, xxv, 52.
121. Grubbs, S. B.: Detection of Hydrocyanic Acid Gas: Use of Small Animals for this Purpose, Pub. Health Rep., Washington, 1917, xxxii, 565-570.
122. Haferkorn, H. E. and Neumann, Felix: Poisonous Gases in Warfare, Application, Prevention, Defense and Medical Treatment, a Short Annotated Bibliography of Gases and Kindred Devices Applied in the Present War, Washington, 1917, Engineer School, 27 p., 8°.
123. Huot: Sur la thérapeutique de l'intoxication par les gaz suffocants, Presse méd., 1917, xxv, 459.
124. Klotz, Oskar: Acute Death from Chlorine Poisoning, Jour. Lab. and Clin. Med., 1917, ii, 889-895.
125. Knack: Kampfgasvergiftungen, Deutsch. med. Wchnschr., 1917, xliii, 1246.
126. —: Schädigungen durch Gasangriffe, München. med. Wchnschr., 1917, lxiv, 880.
127. Kramer O.: Ueber Chlorgasvergiftung, Vrtljschr. f. gerichtl. Med., 1917, Hf. 2; Abst. in Cor.-Bl. f. Schweiz. Aerzte, 1917, xlvii, 987.
128. Kruglevsky, N. A.: [Mechanism of Acute Edema of the Lungs from Poisoning with Asphyxiating Gases.] Russk. Vrach, 1917, xvi, 385; Abst. in Jour. Am. Med. Assn., 1917, lxix, 2005.
129. Leclercq and Mazel: Intoxications oxy-carbonées par projectiles de guerre (formes frustes et formes anormales), Presse méd., 1917, xxv, 395.
130. Leporsky, N. J.: [Behavior of the Vegetative Nervous System During Poisoning from Asphyxiating Gases.] Russk. Vrach, 1917, xvi, 391; Abst. in Jour. Am. Med. Assn., 1917, lxix 2007.
131. Lévy and Tronquet: Un cas d' intoxication par les gaz simulant la tuberculose pulmonaire, Bull. et mém. Soc. méd. d. hôp. de Paris, 1917, 3.s., xli, 824-826.
132. Lian, C.: De l'insuffisance cardiaque, séquelle de l'intoxication par les gaz chlorés, Presse méd., 1917, xxv, 49.
133. LoMonaco, D.: Su un nuevo metodo per la conservazione delle sostanze animali e vegetali con i gas asfissianti, Arch. di farm. sper., Roma, 1917, xxiv, 280-288.
134. Lyon-Caen, L. and Kuss: Pyopneumothorax et gaz asphyxiants, Bull. de l'Acad. de Méd., Paris, 1917, 3.s., lxxviii, 96; also: Pyopneumothorax causé par les gaz asphyxiants, Rev. gén. de clin. et de thérap., 1917, xxxi, 486-488.
135. McNally, W. D.: Carbon Monoxide Poisoning, Jour. Am. Med Assn., 1917, lxix, 1586.
136. Magnus: Kampfgaserkrankungen, Deutsch. med. Wchnschr., 1917, xliii, 221.
137. Miller, J. and Rainy, H.: A Note on the Blood Changes in Gas Poisoning, Lancet, London, 1917, i, 19.
138. Miller, J.: Blood Changes in Gas Poisoning, Lancet, London, 1917, i, 793.
139. Mott, F. W.: Punctiform Haemorrhages of the Brain in Gas Poisoning, Brit. Med. Jour., 1917, i, 637; also: Proc. Roy. Soc. Med., London, 1916-17, x, Sect. Path., 73-90, 3 pl.
140. Natier, M.: [Ozoena and Asphyxiating Gases (new Etiological and Pathogenic Conceptions)] Monde méd., 1917, xxvii, 171-176, also: Ann. Otol. Rhinol. and Laryngol., St. Louis, 1917, xxvi, 942, 1162; also: Tr. Am. Laryngol. Assn., New York, 1917, xxxv, 254-262; also: Virginia Med. Semi-Month., 1918, xlv, 88.
141. Neiding, M. N.: [The Nervous Manifestations with Poisoning from Asphyxiating Gases.] Russk. Vrach, 1917, xvi, 397; Abst. in Jour. Am. Med. Assn., 1917, lxix, 2007.
142. Nicloux, M.: L'instabilité de l'hémoglobine oxycarbonée en présence d'oxygène: son intérêt au point de vue du traitement de l'intoxication oxycarbonée, Presse méd., 1917, xxv, 153.
143. Nicloux, M.: A propos de la note de Ch. Achard, Ch. Flandin et G. Desbouis: Mesure de l'intoxication oxycarbonée par la capacité respiratoire, Compt. rend. Soc. de biol., 1917, lxxx, 521-525.

144. Parisot, J. and Tixier, L.: Les troubles cardiovasculaires consécutifs à l'intoxication par les gaz asphyxiants, Paris méd., 1917, pp. 389-394.

145. Paul, T.: Merkblatt über die ärztliche Behandlung von Personen, die infolge Einatmung der durch feindliche Fliegerbomben entwickelten Gase erkrankt sind, München med. Wchnschr., 1917, lxiv, 167.

146. Pellegrini, R.: Studi suir gas asfissianti; sull' azione dei vapori di bromo, Pensiero med., Milano, 1917, vii, 1, 13, 25.

147. —: Studi sui gas asfissianti; delle alterazioni pancreatiche consecutive ad inalazioni di vapori di bromo; confronto con altre modalità di asfissia, Pensiero med., Milano, 1917, vii, 253-255.

148. —: Studi sui gaz asfissianti. Ricerche istologiche sulle alterazioni polmonari consecutive ad inalazioni di bromo negli animali atropinizzali, Quad. di med. leg., Milano, 1917, i, 305; 1918, ii, 13.

149. —: Un poco noto criterio diagnostico nelle morti per asfissia da gaz deleteri, Arch. di farm. sper., Roma, 1917, xxiii, 201-205.

150. —: Studi sui gaz asfissianti. Ricerche istologiche sulle alterazioni polmonari consecutive ad inalazioni, Arch. di farm. sper., Roma, 1917, xxiv, 58-64.

151. —: [Behavior of Thyroid in Gassing.] Riforma med., 1917, xxxiii, 617.

152. Picca, P.: Prima dei gas asfissianti, Riv. ospedal, Roma, 1917, vii, 584.

153. Piccinini, P.: Per la difesa dei gas asfissianti, Gazz med. di Roma, 1917, xliii, 30-35.

154. Pinard, M.: Gaz toxiques, urticaire et tuberculose, Presse méd., 1917, xxv, 668.

155. Preble, E.: Poison Gases in Warfare, Ref. Handb. Med. Sc., N. Y., 1917, viii, 597.

156. Ramond, Petit and Carrié: Les gastrites aigues consécutives aux intoxications par le gaz, Bull. de la Soc. méd. d. hôp., Paris, 1917, xli, 1169-1173; Abst. in Jour. Am. Med. Assn., 1918, lxx, 962.

157. Ravaut, P. and Réniac: Intoxication par les gaz asphyxiants. Diphtérie secondaire méconnue, Bull. de la Soc. méd. d. hôp., Paris, 1917, xli, 1190-1192; Abst. in Jour. Am. Med. Assn., 1918, lxx, 891.

158. Rumpelmayer: Traitement local, à l'aide du pansement huileux interne, des accidents produits par les gaz chlorés, Bull. de l'Acad. de méd., Paris, 1917, lxxviii, 500.

159. Sereisky, M. Y.: [The Nervous and Psychic Conditions with Poisoning from Asphyxiating Gases.] Russk. Vrach, 1917, xvi, 401; Abst. in Jour. Am. Med. Assn., 1917, lxix, 2007.

160. Stempowski, R.: Traitement de l'intoxication par l'oxychlorure de carbone, Presse méd., 1917, xxv, 523.

161. Tapie, J.: Broncho-pneumonie tuberculeuse aiguë consécutive à une inhalation de gaz asphyxiants, Progrès méd., 1917, 3.s., xxxii, 349.

162. Tizengauzen, M. M.: [Pathologic anatomy of the gassed.] Russk. Vrach, 1917, xvi, 466-468.

163. Ujlski, P.: Beobachtungen bei Gasvergifteten, München med. Wchnschr., 1917, lxiv, 37.

164. Vaughan, V. C.: Editorial—The Use of Poisonous Gases in the Present War, Jour. Lab. and Clin. Med., 1917, iii, 70-74.

165. Voivenel, P. and Martin, P.: Sur les syndromes cliniques de l'intoxication par les gaz suffocants, Progrès, méd., 1917, xxxii, 288; Presse méd., 1917, xxv, 460; Abst. in Jour. Am. Med. Assn., 1917, lxix, 1478.

166. Voivenel, P. and Martin,. P.: La triple courbe de la témperature, du pouls et de la respiration dans l'intoxication par gaz suffocants, Progrès méd., 1917, 3.s., xxxii, 433-436.

167. —Ed.: War Gas Poisoning, Brit. Med. Jour., 1917, ii, 138.

1918.

168. Allen, Walter, C.: Chemical Poisons in Warfare, New York Med. Jour., 1918, cviii, 989-992.

169. Auer, John: Generalized Analgesia in Cats After Exposure to a War-gas, $(CH_3)_2SO_4$, Proc. Soc. Exper. Biol. and Med., 1918, xv, 106.

170. —: Localized Pulmonary Edema in Cats After Inhalation of a War-gas $(CH_3)_2SO_4$, Proc. Soc. Exper. Biol. and Med., 1918, xv, 106.

171. Auld, S. J. M.: Methods of Gas Warfare, Jour. Wash. Acad. Sc., Baltimore, 1918, viii, 45-57; J. Indust. & Engin. Chem., Easton, Pa., 1918, x, 297-301.
Also: Enemy's Methods of Gas Warfare, Jour. Soc. Chem. Indust., Lond., 1918, xxxvii, 127.

172. Barbensi, G.: Disturbi nervosi consecutive all'azione dei gas asfissianti, Riv. crit. di clin. med., Firenze, 1918, xix, 176-178.

173. Brieger, E.: Zur Blutdruckmessung beim Gaskranken. Versuche über den Einfluss einer Viscositätserhöhung des Blutes auf die Blutdruckmessung nach Riva-Rocci, Med. Klin., 1918, xiv, 542-544.

174. Capezzuoli, C.: Toxic Gases in Warfare, Riv. crit. di clin. med., Firenze, 1918, xix, 367; Abst. in Jour. Am. Med. Assn., 1918, lxxi, 1521.

175. Cavazzani, Ernilio: In tema di gas asfissianti e di campi tattilli, II Policlinico, Roma, 1918, xxv, 178-184; Abst. Jour. Am. Med. Assn., 1918, cxxi, 608.

176. CHEYRON: Accidents par inhalations de gaz allemands, Jour. de méd. et chir. prat. 1918, lxxxix, 124-135; Abst. in Rev. War Surg. and Med., 1918, i, No. 5, p. 67.
177. CUMSTON, C. G.: Medical Notes from the Front; [The Pathology, Symptoms and Treatment of the Effects of Asphyxiating Gas.] New York Med. Jour., 1918, cvii, 652-654.
178. DE CONCILIIS: Meccanismo d'azione dei gas asfissianti, Policlinico, Roma, 1918, xxv, 88-96; Abst. in Jour. Am. Med. Assn., 1918, lxx, 1508.
179. DE LUTIIS, E.: Gas asfissianti e loro cura, Incurabili, Napoli, xxxii, 121-127.
180. FLUSSER, E.: Einiges über Kampfgasschädigung, Wien. klin. Wchnschr., 1918, xxxi, 413-415.
181. GIMBERT: Tuberculose et gaz asphyxiants, Paris Méd., 1918, No. 1, pp. 17-23; Abst. Jour. Am. Med. Assn., 1918, lxx, 817.
182. HANS, O.: Zur Klinik der Gasvergiftung, Wien. klin. Wchnschr., 1918, xxxi, 838.
183. KERSHNER, W. E.: Secondary Optic Atrophy Due to "Gassing," Am. Jour. Ophth., St. Louis, 1918, i, 168.
184. LAZENBY, J. M.: Treatment of Irritant Gas Poisoning, Brit. Med. Jour. 1918, ii, 342.
185. LEPAYSANT, P.: Les gaz asphyxiants dans l'antiquité, Chron. méd., Par., 1918, xxv, 256.
186. LISTER, T. D.: The Treatment of Acute Gas Cases, Lancet, London, 1918, i, 617.
187. MILLER, JAMES: A Blood Change in Gas Poisoning, Jour. Roy. Army Med. Corps, Lond., 1918, xxx, 76-87.
188. MOUTIER, F.: Accidents appendiculaires consécutifs à l'intoxication par les gaz chlorés, Arch. d. Mal. d. l'App. Digestif, Paris, 1918, ix, 493; Abst. in Jour. Am. Med. Assn., 1918, lxx, 1505.
189. NICOLAYSEN, N. A.: [Poisoning by Inhalation of Nitrogenous Gases.] Med. Rev., Bergen, 1918, xxxv, 267-282.
190. NORRIS, G. W.: Toxic Gases in Modern Warfare, Jour. Am. Med. Assn., 1918, lxxi, 1822-1825.
191. PEAT, C. B.: The Effects of Gassing as Seen at a Casualty Clearing Station, Canad. M. Assn., Jour., Toronto, 1918, viii, 17-23.
192. PICK, F.: Ueber Erkrankung durch Kampfgase, Wien. klin. Wchnchr., 1918, xxxi, 488.
193. PIERY: [Low Blood Pressure and Tachycardia in Gas Asphyxia.] Lyon Méd., 1918, cxxvii, 321.
194. RANKIN, E.G.: Observations on Gas Poisoning, Med. Rec , New York, 1918, xciv, 942.
195. ROSS, S. G. AND HENDERSON, A. T.: Report on Series of Gassed Cases, Bull. of Can. Army Med. Corps, Ottawa, 1918, i, 58; Abst. in Jour. Am. Med. Assn., 1918, lxxi, 775.
196. ROVERIO, G.: Brevi note sui gas tossici impiegati in guerra e mezzi preventivi o curative, Gior. di med. mil., Roma, 1918, lxvi, 908-919.
197. SAMMARTINO, U.: La gastrite da "gas asfissianti," Arch. di farm. sper., Roma, 1918, xxv, 300-320, 4 pl.
198. SATRE, A. AND GAOS, P.: Deux cas d'insuffisance surrénale aiguë chez des soldats intoxiqués par les gaz, Jour. de méd. et de chir. prat., 1918, lxxxix, 409-416.
199. STOKER, E.: Ozone in Cases of Gassing, Lancet, London, 1918, i, 550.
200. STURSBERG: Kann die chronische Einwirkung nitroser Gase organische Erkrankungen des Zentralnervensystems zur Folge haben? Deutsch. med. Wchnschr., 1918, xliv, 1206.
201. TEDESCHI, E.: Gas asfissianti e tuberculosi pulmonare, Riforma med., 1918, xxxiv, 2; Abst. Jour. Am. Med. Assn., 1918, lxx, 740.
202. TURNER, P.: Case of Sudden Death After an Anesthetic in Latent Case of Shell Gas Poisoning, Lancet, London, 1918, ii, 384.
203. VON ZEYNEK, R.: Ueber Kampfgasvergiftungen, Wien. med. Wchnschr., 1918, lxviii, 1057, 1058.
204. WELLER, C. V.: The Pathology of Gassing, with a Bibliography Upon the Medical Aspects of Gassing, The Int. Assn. of Medical Museums, Bull., 1918, vii, 126-147.
205. ZAGARI: Imponenti gastrorragie da ulcerazioni gastriche, quali effetti dei gas tossici in guerra, Riforma med. 1918, xxiv, 242-245; Abst. in Jour. Am. Med. Assn., 1918, lxx, 1802.
206. —Ed.: Gases in Modern Warfare, Jour. Am. Med. Assn., 1918, lxx, 1160.
207. —Campaign Against Poisonous Gases, Paris Letter, Jour. Am. Med. Assn., 1918, lxxi, 1239.
208. —Ed.: Appendicitis From Gassing, Medical Rec., New York, 1918, xciv, 283.
209. —Gas Poisoning, Rev. War. Surg. and Med., (Prepared in Office of the Surgeon General), 1918, i, 51-57.
210. UNITED STATES: Medical Advisory Board. Chemical Warfare Service. Reports.
211. GREAT BRITAIN: Medical Research Committee. Reports of the Chemical Warfare Medical Committee.

1919

212. ACHARD, C.: [Sequels of Gassing.] Bull. de l'Acad de méd., Paris, 1919, lxxxi, 135.
213. MOREAU, L.: Aspect radiologique des séquelles pulmonaires de l'intoxication par les gaz asphyxiants, Prog. méd., 1919, pp. 191, 192.
214. WINTERNITZ, M. C.: Anatomic Changes in Respiratory Tract Initiated by Irritating Gases, Mil. Surg., 1919, xliv, 476.

C. General References on Use of Gas and Flame in Warfare

1. Auld, S. J. M.: Gas and Flame, G. H. Doran & Co., 1918.
2. Cox, G. H.: Gas Poisoning in Warfare, Med. Rec., New York, 1919, xcv, 312-318.
3. Lewes, V. B.: Poison Gas and Incendiary Bombs, Illustrated London News, July 31, 1915.
4. Neuburger, A.: Chemical Attack.
5. Straight, J. M.: War Rights on Land.
6. Editorial: War Gas Poisoning, Brit. Med. Jour., 1918, ii, 138-139.
7. Nasmith, G. G.: Poison Gases in Warfare, Med. Rec., New York, 1919, xcvi, 146-157.

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